FILE 'REGISTRY' ENTERED AT 14:50:34 ON 18 MAY 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 17 MAY 2009 HIGHEST RN 1147079-26-2
DICTIONARY FILE UPDATES: 17 MAY 2009 HIGHEST RN 1147079-26-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2009.

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

L1 20 S "A1-ANTITRYPSIN"?/CN

FILE 'HCAPLUS' ENTERED AT 14:50:35 ON 18 MAY 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 18 May 2009 VOL 150 ISS 21
FILE LAST UPDATED: 17 May 2009 (20090517/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2009

HCAplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2008.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate
substance identification.

L1 20 SEA FILE=REGISTRY ABB=ON PLU=ON "A1-ANTITRYPSIN"?/CN
L2 10337 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 OR (A1 OR ALPHA1 OR

```
                (ALPHA OR A)(1A)1)(A)(ANTITRYPSIN OR ANTI(W)(TRYPSIN OR
                PROTEINASE OR PROTEASE) OR ANTIPROTEASE OR ANTIPROTEINASE
                OR (PROTEASE OR PROTEINASE)(W)INHIBIT?) OR A1PI OR
                PROLASTIN OR ZEMAIRA OR AAT(10A)?TRYPSIN? OR A1AT OR
                ANTITRYPSIN OR ANTI TRYPSIN
L3          392 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L2(30A)(ADMIN? OR INJECT?
                OR APPLY? OR APPLIED OR APPLICATION)
L4           73 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3(30A)(PARENTAL? OR
                ORAL? OR MOUTH OR VAGINAL? OR RECTAL? OR ANAL OR NASAL? OR
                MOSE OR BUCCAL? OR INTRAVENOUS? OR IV OR I V OR INTRA(W)(VE
                NOUS? OR MUSCUL? OR CEREBROVENTRIC?) OR INTRAMUSCUL? OR
                SUBCUTANEOUS? OR INTRATHECAL? OR EPIDURAL? OR TRANSDERMAL?
                OR INTRACEREBROVENTRIC?)



L1           20 SEA FILE=REGISTRY ABB=ON  PLU=ON  "A1-ANTITRYPSIN"?/CN
L2        10337 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 OR (A1 OR ALPHA1 OR
                (ALPHA OR A)(1A)1)(A)(ANTITRYPSIN OR ANTI(W)(TRYPSIN OR
                PROTEINASE OR PROTEASE) OR ANTIPROTEASE OR ANTIPROTEINASE
                OR (PROTEASE OR PROTEINASE)(W)INHIBIT?) OR A1PI OR
                PROLASTIN OR ZEMAIRA OR AAT(10A)?TRYPSIN? OR A1AT OR
                ANTITRYPSIN OR ANTI TRYPSIN
L3          392 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L2(30A)(ADMIN? OR INJECT?
                OR APPLY? OR APPLIED OR APPLICATION)
L5            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3(30A)(OSMOTIC?(W)PUMP
                OR INHALE# OR INHALANT OR INHALING OR INHALATION?)



L6           46 SEA ABB=ON  PLU=ON  (L4 OR L5) AND (PY<2000 OR AY<2000 OR PRY<2000)
L7           37 SEA ABB=ON  PLU=ON  L6 AND (PARENTAL? OR ORAL? OR MOUTH OR
                INTRAVENOUS? OR IV OR I V OR INTRA(W)(VENOUS? OR MUSCUL?)
                OR INTRAMUSCUL? OR EPIDURAL?)
L8            9 SEA ABB=ON  PLU=ON  L6 NOT L7

L8   ANSWER 1 OF 9  HCAPLUS  COPYRIGHT 2009 ACS on STN
ED   Entered STN:  22 May 2003
ACCESSION NUMBER:         2003:390758  HCAPLUS  Full-text
DOCUMENT NUMBER:          138:390934
TITLE:                    Topical and transdermal administration of peptidyl
                          drugs with hydroxide-releasing agents as skin
                          permeation enhancers
INVENTOR(S):              Luo, Eric C.; Jacobson, Eric C.; Hsu, Tsung-Min
PATENT ASSIGNEE(S):       Dermatrends, Inc., USA
SOURCE:                   U.S., 13 pp., Cont.-in-part of U.S. Ser. No.
                          569,889.
                          CODEN: USXXAM
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   26
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
     ----------------    ----   --------    ---------------------   --------
     US 6565879           B1    20030520    US 2000-687937          20001013
                                                    <--
     US 20010038862       A1    20011108    US 2000-737831          20001214
                                                    <--
     US 6558695           B2    20030506
     ZA 2002004671        A     20030611    ZA 2002-4671            20020611
```

Query as specified wherein ans. set limited to patent/non-patent citations dated prior 2000

			<--	
US 20030147943	A1	20030807	US 2003-349582	20030122
			<--	
PRIORITY APPLN. INFO.:			US 1999-465098	A2 19991216
			<--	
			US 2000-569889	A2 20000511
			US 2000-687937	A2 20001013
			US 2000-737831	A3 20001214

AB A method is provided for increasing the permeability of skin or mucosal tissue to a topically or transdermally administered pharmacol. or cosmeceutically active peptide, polypeptide or protein. The method involves use of a specified amount of a hydroxide-releasing agent, the amount optimized to increase the flux of the peptide, polypeptide or protein through a body surface while minimizing the likelihood of skin damage, irritation or sensitization. Formulations and drug delivery devices employing hydroxide-releasing agents as permeation enhancers are provided as well. An in vitro human cadaver skin permeation study was conducted using 0.18% leuprolide solution and 3.6% sodium hydroxide.

IT 9041-92-3, α1-Antitrypsin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(topical and transdermal administration of peptidyl drugs with hydroxide-releasing agents as skin permeation enhancers)

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 09 Nov 2001
ACCESSION NUMBER: 2001:817206 HCAPLUS Full-text
DOCUMENT NUMBER: 135:362582
TITLE: Topical and transdermal administration of peptide drugs using hydroxide releasing agents as permeation enhancers
INVENTOR(S): Luo, Eric C.; Hsu, Tsung-Min
PATENT ASSIGNEE(S): Dermatrends, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp., Cont.-in-part of U.S. Ser. No. 687,937.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 26
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20010038862	A1	20011108	US 2000-737831	20001214
			<--	
US 6558695	B2	20030506		
US 6565879	B1	20030520	US 2000-687937	20001013
			<--	
ZA 2002004671	A	20030611	ZA 2002-4671	20020611
			<--	
US 20030147943	A1	20030807	US 2003-349582	20030122
			<--	
PRIORITY APPLN. INFO.:			US 1999-465098	A2 19991216
			<--	

US 2000-569889 A2 20000511

US 2000-687937 A2 20001013

US 2000-737831 A3 20001214

AB A method is provided for increasing the permeability of skin or mucosal tissue to a topically or transdermally administered pharmacol. or cosmeceutically active peptide, polypeptide or protein. The method involves use of a specified amount of a hydroxide-releasing agent, the amount optimized to increase the flux of the peptide, polypeptide or protein through a body surface while minimizing the likelihood of skin damage, irritation or sensitization. Formulations and drug delivery devices employing hydroxide-releasing agents as permeation enhancers are provided as well. The in-vitro permeation of oxytocin through human cadaver skin was performed by using Franz-type diffusion cells with a diffusion area of 1 cm2. The cumulative amount of oxytocin across human cadaver skin was calculated by using the measured oxytocin concns. in the receiver solns. for each time point.

IT 9041-92-3, α1-Antitrypsin
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(topical and transdermal administration of peptide drugs using hydroxide releasing agents as permeation enhancers)

L8 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 14 Dec 1998
ACCESSION NUMBER: 1998:778179 HCAPLUS Full-text
DOCUMENT NUMBER: 130:121266
TITLE: Kinetic analysis of enzyme inactivation under second-order conditions by use of substrate-to-product progress curves: application to the inhibition of trypsin by α-1 proteinase inhibitor
AUTHOR(S): Ozer, Inci
CORPORATE SOURCE: Department of Biochemistry, School of Pharmacy, Hacettepe University, Ankara, 06100, Turk.
SOURCE: Analytical Biochemistry (1998), 264(2), 199-203
CODEN: ANBCA2; ISSN: 0003-2697
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The inhibition of bovine pancreatic trypsin by human α-1 proteinase inhibitor (α-1 PI) was studied under second-order conditions by continuously monitoring the fluorescence change due to the enzymic hydrolysis of N-α-benzoyl-L-arginine 7-amido-4-methylcoumarin as substrate. Employing equimolar starting concns. of enzyme and inhibitor (110-220 nM), the fluorescence progress curve was analyzed according to the equation Pt = (kcat[S]/kiKm)ln{ki[E]0t + 1}, where ki is the second-order rate constant for the reaction, E + α-1 PI → E*α-1 PI (inactive). Ki was found to be 1.8 ± 0.16 + 107 M-1 min-1 (at pH 7.0 and 25°), in close agreement with results obtained by alternative kinetic methods. The method reported appears to be valid and should be useful in the study of fast reactions where one of the reaction partners is an enzyme. An extension of the second-order progress curve approach to cover non-equimolar mixts. of E and I is also offered. (c) 1998 Academic Press.

IT 9041-92-3
RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); BIOL (Biological study)
(kinetic anal. of enzyme inactivation under second-order conditions by use of substrate-to-product progress curves and application to inhibition of trypsin by α-1 proteinase inhibitor)

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 22 Jan 1998
ACCESSION NUMBER: 1998:35384 HCAPLUS Full-text
DOCUMENT NUMBER: 128:113455
ORIGINAL REFERENCE NO.: 128:22217a,22220a
TITLE: Clinical application of genetic engineering in analysis of respiratory organ diseases
AUTHOR(S): Kikuchi, Toshiaki; Nukiwa, Toshihiro
CORPORATE SOURCE: Res. Inst. Gerontol., Tohoku Univ., Sendai, 980-77, Japan
SOURCE: Medicina (Tokyo) (1997), 34(12), 2142-2144
CODEN: MDCHBH; ISSN: 0025-7699
PUBLISHER: Igaku Shoin Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review with 3 refs., on the theory of elastase-antielastase unbalance and α1-antitrypsin deficiency.
IT 9041-92-3, α1-Antitrypsin
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(clin. application of genetic engineering in anal. of respiratory organ diseases)

L8 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 17 Sep 1994
ACCESSION NUMBER: 1994:530943 HCAPLUS Full-text
DOCUMENT NUMBER: 121:130943
ORIGINAL REFERENCE NO.: 121:23609a,23612a
TITLE: Effects of porcine pancreatic elastase-1 on elastin in human trabecular meshwork. -Immunohistochemical studies: Report 2-
AUTHOR(S): Hoya, Takuo
CORPORATE SOURCE: Dep. Ophthalmol., Shinshu Univ. Sch. Med., Matsumoto, 390, Japan
SOURCE: Nippon Ganka Gakkai Zasshi (1994), 98(1), 13-22
CODEN: NGZAA6; ISSN: 0029-0203
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB The aim of this study was to confirm the penetration of porcine pancreatic elastase-1 (PPE) into the aqueous humor and trabecular tissue through blood vessels. First, .alpha.1- antitrypsin-elastase complex (α1 A-EL) was administered to rats to determine the penetration of α1A-EL into the trabecular tissue by light microscopic anal. with immunohistochem. and by electron microscopic anal. with protein A-gold immunohistochem. staining. Secondly, the penetration of PPE into the aqueous humor of the patients given PPE was estimated by Western blot anal. Finally, human trabecular tissues were sectioned for electron microscopy. The sections were soaked in the aqueous humor and the changes of immunolocalization of elastin in the tissues

was evaluated with protein A-gold immunohistochem. staining. The trabecular tissues of the α1A-EL-treated rats showed a pos. immunoreaction under the light microscope, and labeling by gold particles was demonstrated in the trabecular tissues by electron microscope. Western blot anal. proved that there was α1A-EL in the aqueous humor obtained from PPE-administered patients, but not in the aqueous humor of control patients. The gold particles showing the presence of elastin were less abundant in the specimens exposed to the aqueous humor of PPE-administered patients than in that of control patients.

L8 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 13 Dec 1992
ACCESSION NUMBER: 1992:631189 HCAPLUS Full-text
DOCUMENT NUMBER: 117:231189
ORIGINAL REFERENCE NO.: 117:39925a,39928a
TITLE: Molecular biology of the genes of respiratory disorders. Application of gene analysis and genetic engineering
AUTHOR(S): Nukiwa, Toshihiro
CORPORATE SOURCE: Sch. Med., Juntendo Univ., Tokyo, 113, Japan
SOURCE: Saishin Igaku (1992), 47(Suppl.), 1654-78
CODEN: SAIGAK; ISSN: 0370-8241
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review, with 71 refs., on the gene anal. in .alpha .1-antitrypain deficiency and cystic fibrosis and application of genetic engineering to treatment of these diseases.

L8 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 27 Jun 1992
ACCESSION NUMBER: 1992:248421 HCAPLUS Full-text
DOCUMENT NUMBER: 116:248421
ORIGINAL REFERENCE NO.: 116:41915a,41918a
TITLE: Treatment of pulmonary inflammation with α1-antitrypsin
INVENTOR(S): Lezdey, John; Wachter, Allan
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 3 pp. Cont.-in-part of U.S. 5,008,242.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5093316	A	19920303	US 1990-591757 <--	19901002
US 5008242	A	19910416	US 1989-445005 <--	19891204
CA 2019974	A1	19910604	CA 1990-2019974 <--	19900627
CA 2019974	C	20020122		
EP 432117	A1	19910612	EP 1990-850286 <--	19900829
EP 432117	B1	19940622		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE

ES 2055406	T3	19940816	ES 1990-850286 <--	19900829
JP 03181422	A	19910807	JP 1990-238844 <--	19900906
PRIORITY APPLN. INFO.:			US 1986-946445 <--	B2 19861224
			US 1988-181707 <--	B2 19880414
			US 1988-242735 <--	B2 19880909
			US 1989-445005 <--	A2 19891204

AB Symptoms of pulmonary inflammation in pulmonary disease which express proteases are treated by administering an effective amount of microcryst. .alpha.1-antitrypsin, or its derivs. or salts, by inhalation whereby elastase and cathepsin G are controlled. Formulations of microcryst. α1-antitrypsin are described.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1976:507184 HCAPLUS Full-text
DOCUMENT NUMBER: 85:107184
ORIGINAL REFERENCE NO.: 85:17197a,17200a
TITLE: The role of sialic acid in hepatic uptake of alpha1-antitrypsin
AUTHOR(S): Fierer, Joshua A.; Sampson, Phyllis; Mandl, Ines
CORPORATE SOURCE: Coll. Physicians Surg., Columbia Univ., New York, NY, USA
SOURCE: Protides of the Biological Fluids (1976), Volume Date 1975, 23, 119-23
CODEN: PBFPA6; ISSN: 0079-7065
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The role of sialic acid in liver metabolism of .alpha.1 -antitrypsin in .alpha.1-antitrypsin deficiency was studied by injection into rats of .alpha.1-antitrypsin, desialylated .alpha.1-antitrypsin, and . alpha.1-antitrypsin from a patient with . alpha.1-antitrypsin deficiency, with subsequent anal. of the liver. The desialylated α1-antitrypsin and the α1-antitrypsin of patients with α1-antitrypsin had similar liver uptake patterns.

L8 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 16 Dec 2001
ACCESSION NUMBER: 1915:3174 HCAPLUS Full-text
DOCUMENT NUMBER: 9:3174
ORIGINAL REFERENCE NO.: 9:482h-i
TITLE: Enzyme act on. XVIII. Lipoids as inhibitors of anaphylactic shock
AUTHOR(S): Jobling, James W.; Petersen, Wm.
CORPORATE SOURCE: Columbia Univ.
SOURCE: Journal of Experimental Medicine (1914), 20, 468-76
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB The antitryptic titer of the serum can be increase by subcutaneous injections of serum lipoids (antitrypsin) and of the lipoids from egg yolk. Animals so injected show a relative immunity to acute anaphylactic shock (2 minimum lethal doses). Extraction of lipoids contained in antigens increases the toxicity of the antigen when injected into a sensitized animal. Sublethal doses of soap solns. injected simultaneously with the antigen (purified horse serum albumin) prevent anaphylactic shock. The refractory state following anaphylactic shock is related in part to an increase in the antitryptic titer of the serum.

FILE 'MEDLINE' ENTERED AT 14:50:36 ON 18 MAY 2009

FILE 'BIOSIS' ENTERED AT 14:50:36 ON 18 MAY 2009
Copyright (c) 2009 The Thomson Corporation

FILE 'EMBASE' ENTERED AT 14:50:36 ON 18 MAY 2009
Copyright (c) 2009 Elsevier B.V. All rights reserved.

FILE 'WPIX' ENTERED AT 14:50:36 ON 18 MAY 2009
COPYRIGHT (C) 2009 THOMSON REUTERS

FILE 'JAPIO' ENTERED AT 14:50:36 ON 18 MAY 2009
COPYRIGHT (C) 2009 Japanese Patent Office (JPO)- JAPIO

FILE 'PASCAL' ENTERED AT 14:50:36 ON 18 MAY 2009
Any reproduction or dissemination in part or in full,
by means of any process and on any support whatsoever
is prohibited without the prior written agreement of INIST-CNRS.
COPYRIGHT (C) 2009 INIST-CNRS. All rights reserved.

FILE 'DISSABS' ENTERED AT 14:50:36 ON 18 MAY 2009
COPYRIGHT (C) 2009 ProQuest Information and Learning Company; All Rights Res
erved.

FILE 'LIFESCI' ENTERED AT 14:50:36 ON 18 MAY 2009
COPYRIGHT (C) 2009 Cambridge Scientific Abstracts (CSA)

FILE 'BIOTECHDS' ENTERED AT 14:50:36 ON 18 MAY 2009
COPYRIGHT (C) 2009 THOMSON REUTERS

FILE 'SCISEARCH' ENTERED AT 14:50:36 ON 18 MAY 2009
Copyright (c) 2009 The Thomson Corporation

FILE 'BIOTECHABS' ACCESS NOT AUTHORIZED

FILE 'BIOTECHNO' ENTERED AT 14:50:36 ON 18 MAY 2009
COPYRIGHT (C) 2009 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'PROMT' ENTERED AT 14:50:36 ON 18 MAY 2009
COPYRIGHT (C) 2009 Gale Group. All rights reserved.

FILE 'RDISCLOSURE' ENTERED AT 14:50:36 ON 18 MAY 2009
COPYRIGHT (C) 2009 Kenneth Mason Publications Ltd.

L9 29 S L8
L10 21 DUP REM L9 (8 DUPLICATES REMOVED)

L10 ANSWER 1 OF 21 WPIX COPYRIGHT 2009 THOMSON REUTERS on STN
ACCESSION NUMBER: 2000-637643 [61] WPIX

DOC. NO. CPI: C2000-191764 [61]
TITLE: Treatment of a patient suffering from a non-pulmonary disease e.g. diabetes comprises administration of polypeptides and a protease inhibitor by inhalation
DERWENT CLASS: B04
INVENTOR: LEZDEY J; WACHTER A
PATENT ASSIGNEE: (LEZD-I) LEZDEY J; (WACH-I) WACHTER A
COUNTRY COUNT: 1

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 6124257	A	20000926	(200061)*	EN	3[0]	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 6124257 A	CIP of	US 1997-922120	19970828
US 6124257 A		US 1998-201608	19981130

PRIORITY APPLN. INFO: US 1998-201608 19981130
US 1997-922120 19970828
AN 2000-637643 [61] WPIX
AB US 6124257 A UPAB: 20050411
NOVELTY - Treating a patient suffering from non-pulmonary disease comprising inhalation of a polypeptide (1) and a protease inhibitor (2), is new.
ACTIVITY - Cardiant; antiinflammatory; immunosuppressive; antibacterial; antidiabetic; hypertensive.
MECHANISM OF ACTION - Protease inhibitor.
USE - To treat non-pulmonary diseases e.g. diabetes (claimed), sepsis syndrome, ARDS, RDS, heart attack.
ADVANTAGE - Pulmonary administration of polypeptides is safe and effective. (2) improves the action of the primary drug, inactivates or removes elastase from the lungs thus improving the efficacy of the polypeptides.

L10 ANSWER 2 OF 21 PROMT COPYRIGHT 2009 Gale Group on STN

ACCESSION NUMBER: 1999:238845 PROMT Full-text
TITLE: AlphaOne Pharmaceuticals, Inc. Announces Appointment of New Chairman and Chief Executive Officer.
SOURCE: PR Newswire, (23 Apr 1999) pp. 1809.
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 362
FULL TEXT IS AVAILABLE IN THE ALL FORMAT
AB ALAMEDA, Calif., April 23 /PRNewswire/ -- AlphaOne Pharmaceuticals, Inc. today announced the appointment of Dr. Martin Preuveneers as Chief Executive Officer. Dr. Preuveneers has also taken the position of Chairman of the Board of Directors. During his career, Dr. Preuveneers has held senior management positions at Glaxo Wellcome, including worldwide head of marketing for respiratory products and also, the gastrointestinal product, Zantac(TM). In addition, Dr. Preuveneers has extensive experience in the U.K. biotechnology industry, including being Chief Executive for the gene therapy company Cobra Therapeutics.
THIS IS THE FULL TEXT: COPYRIGHT 1999 PR Newswire Association, Inc.

L10 ANSWER 3 OF 21 PROMT COPYRIGHT 2009 Gale Group on STN

ACCESSION NUMBER: 1998:61636 PROMT Full-text
TITLE: AlphaOne Pharmaceuticals, Inc. Announces the Appointment of Ian C. Bathurst, Ph.D. as Vice President, Process Development and Manufacturing
SOURCE: PR Newswire, (2 Feb 1998) pp. 0202FLM002.
LANGUAGE: English
WORD COUNT: 364
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB ALAMEDA, Calif., Feb. 2 /PRNewswire/ -- AlphaOne Pharmaceuticals, Inc. announced the appointment of Ian C. Bathurst, Ph.D. to the position of Vice President, Process Development and Manufacturing. Dr. Bathurst was formerly with LXR Biotechnology of Richmond, CA, and Chiron Corporation of Emeryville, CA.
AlphaOne Pharmaceuticals, Inc. is a biopharmaceutical company dedicated to the production of recombinant alpha 1 -antitrypsin (AAT or alpha 1-proteinase inhibitor) for inhalation therapy and topical application. The primary indication for the use of its flagship product NEOLASTIN(TM) is in the treatment of hereditary emphysema. Additional potential target indications for NEOLASTIN(TM) include asthma, cystic fibrosis, chronic bronchitis, and emphysema acquired environmentally through cigarette smoke and other airborne pollutants. The only treatment available currently for the long-term treatment of chronic emphysema is an infused human plasma-derived product which is limited in supply. Dermatological targets for DERMOLASTIN(TM), the company's topical formulation of recombinant AAT, include atopic dermatitis and psoriasis. AlphaOne has acquired exclusive worldwide patent rights for the use of recombinant AAT in inflammatory disorders of the lung and skin from Protease Sciences of Tempe, Arizona. AlphaOne's President and COO, Philip J. Barr, Ph.D. said, "Dr. Bathurst brings with him a tremendous amount of experience in the production of clinical grade biopharmaceuticals and their introduction into human clinical trials. This experience will be invaluable as we pursue our aggressive schedule for the clinical development of NEOLASTIN(TM) and DERMOLASTIN(TM)." This news release contains forward-looking statements that involve risks and uncertainties, including risks associated with clinical development, regulatory approvals, product commercialization and other risks described from time to time in offering documents prepared by AlphaOne. An electronic version of this news release, as well as additional information about AlphaOne, of interest to investors, customers, future employees and patients is available on the AlphaOne home page at http://www.alphalpharm.com /CONTACT: Philip J. Barr, Ph.D. President and Chief Operating Officer, or David M. Kent, Chief Financial Officer, both of AlphaOne Pharmaceuticals, 510-337-1250/

L10 ANSWER 4 OF 21 PROMT COPYRIGHT 2009 Gale Group on STN

ACCESSION NUMBER: 1998:413310 PROMT Full-text
TITLE: AlphaOne Pharmaceuticals announces issuance of alpha 1-antitrypsin patent for use in respiratory distress syndrome
SOURCE: BIOTECH Patent News, (1 Jul 1998) pp. N/A.
ISSN: 0898-2813.
LANGUAGE: English
WORD COUNT: 401
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB AlphaOne Pharmaceuticals, Inc. (Alameda, CA; 510-337-1250) announced the issuance of their in-licensed United States patent for the treatment of

respiratory distress syndrome using alpha 1-antitrypsin. The patent covers the use of alpha 1-antitrypsin for both neonatal and adult respiratory distress syndrome. This patent will be added to AlphaOne's existing in-licensed patent portfolio of 14 issued United States patents related to alpha 1-antitrypsin and other protease inhibitors. The patents cover both inhalation and topical administration of alpha 1-antitrypsin for the treatment of pulmonary and dermatological diseases.
Neonatal respiratory distress syndrome is a disease affecting 1 out of every 1,000 births in the United States The disease is marked by high levels of lung degradative enzymes such as elastase, leading to respiratory failure with a 50% mortality rate. Neonatal respiratory distress syndrome is found predominantly among premature infants. "Neonatal respiratory distress syndrome is an area that we feel is very important," stated AlphaOne's chief operating officer, Dr. Philip J. Barr. "We are encouraged by the scientific community's research in this area and intend to continue the development of this important therapy."
AlphaOne's flagship indication is hereditary emphysema, a pulmonary disease also marked by uncontrolled elastase activity. Up to 200,000 individuals in the United States and Europe may suffer from hereditary emphysema, which results frequently in severe morbidity and reduction in lifespan. Hereditary emphysema is treated by infused plasma-derived alpha 1-antitrypsin. Currently, however, less than 10% of the potential worldwide market is being met by the plasma-derived product. The disease is marked by inflammation of the lung, excess proteolytic tissue degradation, and breathing difficulties due to loss of lung function.

L10 ANSWER 5 OF 21 PROMT COPYRIGHT 2009 Gale Group on STN

ACCESSION NUMBER: 1998:283866 PROMT Full-text
TITLE: Gene therapy, alpha-1-antitrypsin GeneMedicine, Vanderbilt University clinical data
SOURCE: R & D Focus Drug News, (15 Jun 1998) pp. N/A.
ISSN: 1350-1135.
LANGUAGE: English
WORD COUNT: 141
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB Results of a phase I study with GeneMedicine's alpha- 1-antitrypsin (AAT) gene therapy for the treatment of AAT deficiency have been reported by Vanderbilt University (USA). Intranasal administration of the gene therapy was well tolerated in five patients and increased levels of the AAT protein were seen in nasal lavage fluid. Levels of AAT peaked 3-5 days following treatment and remained at elevated levels for one week. The gene therapy also had an anti-inflammatory effect that was not observed when the AAT protein was administered to the same patients. The gene therapy was delivered using DOTMA, a cationic lipid delivery system originally developed by Roche and licensed to GeneMedicine. Gene therapy, alpha-1-antitrypsin, gene therapy, alpha-1-antitrypsin/lipid formulation, R7X, All Other Respiratory System Products, GeneMedicine, clinical-data. Gene therapy, alpha-1-antitrypsin, gene therapy, alpha-1-antitrypsin/lipid formulation, R7X, All Other Respiratory System Products, Vanderbilt University, clinical-data.

L10 ANSWER 6 OF 21 PASCAL COPYRIGHT 2009 INIST-CNRS. ALL RIGHTS RESERVED. on STN DUPLICATE 1
ACCESSION NUMBER: 1998-0403995 PASCAL Full-text
COPYRIGHT NOTICE: Copyright .COPYRGT. 1998 INIST-CNRS. All rights reserved.

TITLE (IN ENGLISH): Use of heparin in the treatment of protein-losing enteropathy after Fontan operation for complex congenital heart disease
AUTHOR: KELLY A. M.; FELDT R. H.; DRISCOLL D. J.; DANIELSON G. K.
CORPORATE SOURCE: Department of Pediatric and Adolescent Medicine, Mayo Clinic Rochester, Rochester, Minnesota, United States; Section of Pediatric Cardiology, Mayo Clinic Rochester, Rochester, Minnesota, United States; Division of Thoracic and Cardiovascular Surgery, Mayo Clinic Rochester, Rochester, Minnesota, United States
SOURCE: Mayo Clinic proceedings, (1998), 73(8), 777-779, 13 refs.
ISSN: 0025-6196 CODEN: MACPAJ
DOCUMENT TYPE: Journal; (case report, clinical case)
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: INIST-3250, 354000072790610110
AN 1998-0403995 PASCAL Full-text

AB Protein-losing enteropathy (PLE) is a serious complication of the Fontan operation and is associated with pronounced mortality. Medical management of PLE has been only partially successful. A recent report noted dramatic improvement in patients with PLE within 3 weeks of subcutaneous administration of heparin. We report a case of reversal of PLE with resolution of clinical symptoms and normalization of serum albumin, total protein, and fecal α.sub.1-antitrypsin values after several months of heparin treatment. Our findings substantiate those recently reported but suggest that reversal of PLE may necessitate more than a few weeks of heparin therapy.

L10 ANSWER 7 OF 21 PROMT COPYRIGHT 2009 Gale Group on STN

ACCESSION NUMBER: 97:101660 PROMT Full-text
TITLE: Inhale Therapeutic Systems Announces Fourth Quarter and Year Ended 1996 Financial Results
SOURCE: News Release, (31 Jan 1997) pp. N/A.
LANGUAGE: English
WORD COUNT: 1330
FULL TEXT IS AVAILABLE IN THE ALL FORMAT
AB Palo Alto, Calif., January 31, 1997 - Inhale Therapeutic Systems (NASDAQ:INHL) today announced its financial results for the fourth quarter and year ended December 31, 1996. The Company reported contract research revenues of $2.2 million for the three months ended December 31, 1996, compared to $0.8 million in the same period of 1995. For the year ended December 31, 1996, contract research revenues were $6.9 million compared to $3.4 million last year. The increase is due primarily to revenues received under the Company's agreement with Baxter Healthcare Corporation (see below). For the three months ended December 31, 1996, the Company reported a net loss of $3.3 million or $0.28 per share, compared to a net loss of $2.2 million or $0.22 per share in 1995. For the year ended December 31, 1996, the Company reported a net loss of $9.9 million or $0.88 per share, compared to a net loss of $7.7 million or $0.78 per share, in 1995. The increased loss is due primarily to .Inhale's expansion of its technology development programs. Twelve-Month Summary During the past year, the Company has entered into strategic relationships with four new collaborative partners, moved the pulmonary insulin product development program into a Phase IIb clinical trial and two additional product development programs into Phase I testing, strengthened its balance sheet by adding $25

million of equity financing from corporate partners, and expanded its technology and manufacturing development activities as well as its management team. To date, Inhale has 15 programs in various stages of feasibility, pre-clinical and clinical development, - with four in human clinical trials and ten sponsored by partners. Corporate Collaborations In March 1996, Inhale and Baxter entered into a broad strategic partnership to use Inhale's dry powder pulmonary delivery system as a technology platform for developing and launching therapeutic products. In April 1996, Baxter made a $20 million equity investment in Inhale at a 25% market premium based on the average market price prior to the signing of the agreement. Baxter will receive worldwide commercialization rights in exchange for research and development funding and milestone payments for the first four molecules, estimated at up to $60 million. Baxter also has an option to add molecules to the collaboration that could result in additional funding and milestone payments to Inhale. THIS IS AN EXCERPT: COPYRIGHT 1997 Opus Research

L10 ANSWER 8 OF 21 WPIX COPYRIGHT 2009 THOMSON REUTERS on STN
ACCESSION NUMBER: 1993-188533 [23] WPIX
CROSS REFERENCE: 1992-096256
DOC. NO. CPI: C1993-083504 [23]
TITLE: Mast cell implicated pulmonary disease treatment - by administering mixture of alpha 1-anti trypsin and corticosteroid by inhalation
DERWENT CLASS: B01; B04
INVENTOR: LEZDEY J; WACHTER A J
PATENT ASSIGNEE: (LEZD-I) LEZDEY J
COUNTRY COUNT: 1

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 5215965	A	19930601	(199323)*	EN	9	

<--

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5215965 A	CIP of	US 1990-591752	19901002
US 5215965 A		US 1991-755300	19910905

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 5215965 A	CIP of	US 5093316 A

PRIORITY APPLN. INFO: US 1991-755300 19910905
US 1990-591752 19901002
AN 1993-188533 [23] WPIX
CR 1992-096256
AB US 5215965 A UPAB: 20050509
The factor (DNTF) (i) comprises a polypeptide of mol. weight 9,000-10,000 daltons, is capable of increasing the survival time of foetal, non-mitotic dopamine nerve cells in culture, increases in vivo expression of tyrosine hydroxylase (TH) in substantia migra dopamine nerve cells exposed to the factor, and has a neurotrophic effect on substantia nigra dopamine nerve

cells. Pref purified form of soluble DNTF is derived from cultured cells of the mammalian peripheral nervous system, and comprises a polypeptide having an N-terminal portion with the sequence (I) Xaa-Glu-Asp-Thr-Ser-Asn- Ile-Ala-Val-Ser-Gly-Xaa-Xaa-Pro (Xaa= an aminoacid of mammalian proteins and above characteristics. USE/ADVANTAGE - Increases the survival and function of dopamine nerve cells located in the substantia nigra and projecting to the striatum and, opt. cause regeneration of these cells. The DNTF is used for treating Parkinson's disease. It will inhibit or halt the progress of the disease by reducing the degeneration and dysfunction of substantia nigra nerve cells. Also the DNTF treatment may be used in transplantation strategies where dopamine cells are transplanted for replacing lost dopamine functionan

L10 ANSWER 9 OF 21 LIFESCI COPYRIGHT 2009 CSA on STN
ACCESSION NUMBER: 94:45014 LIFESCI Full-text
TITLE: Treatment of inflammation
AUTHOR: Lezdey, J.; Wachter, A.J.
CORPORATE SOURCE: 976 Kingston Dr., Chery Hill, NJ 08034, USA
SOURCE: (1993) . US Patent 5,215,965.
DOCUMENT TYPE: Patent
FILE SEGMENT: W2; W3
LANGUAGE: English
AB A method for the prophylaxis or direct treatment of mast cell implicated pulmonary disease in mammals which comprises administering by inhalation a composition of a synergistically effective amount of a corticosteroid and a natural or recombinant alpha 1-antitrypsin which inhibits the degranulation of mast cells and/or has an affinity to basophils, the mediators of mast cells or T-cells.

L10 ANSWER 10 OF 21 WPIX COPYRIGHT 2009 THOMSON REUTERS on STN
ACCESSION NUMBER: 1992-331722 [40] WPIX
CROSS REFERENCE: 2001-433094
DOC. NO. CPI: C1992-147521 [40]
TITLE: Somatic cell gene therapy - by implanting transduced skin fibroblasts into loose connective tissue, fixed in extracellular matrix or efficient expression and distribution of required gene prods.
DERWENT CLASS: B04; D16
INVENTOR: ST LOUIS D C; VERMA I M
PATENT ASSIGNEE: (SALK-C) SALK INST BIOLOGICAL STUDIES
COUNTRY COUNT: 17

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 9215676 <--	A1	19920917	(199240)*	EN	54[5]	
US 6645942	B1	20031111	(200382)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9215676 A1		WO 1992-US1890	19920306
US 6645942 B1	CIP of	US 1988-187214	19880428
US 6645942 B1	Cont of	US 1991-667169	19910308
US 6645942 B1		US 1994-232452	19940422

PRIORITY APPLN. INFO: US 1991-667169 19910308
US 1988-187214 19880428
US 1994-232452 19940422
AN 1992-331722 [40] WPIX
CR 2001-433094
AB WO 1992015676 A1 UPAB: 20050820
Method comprises implanting, in the losse connective tissue of the derivs. of a subject to be treated, transduced fibroblasts containing exogenous genetic material, especially under the expression control of a constitutive promoter. Also claimed are skin fibroblasts that have been transduced to be capable of expressing exogeneous genetic material which is maintained under the expression control of a constitutive promoter. The fibroblasts are suitable for implantation into the loose connective tissue of the dervis. of a mammalian receipient. USE/ADVANTAGE - Because the fibroblasts are implanted in a highly vascularised compartment of the skin, the transduced cells and thus their 'replacement' gene products, have direct access to the circulatory system. As a result, the required products can be easily and efficiently be distributed to other parts of the body. When the gene therapy is not longer needed, the implanted fibroblasts can be conveniently removed. In order to overcome prior art problems of inefficient expression, skin fibroblasts are infected with a chimeric retrovirus containing a functionally active endogeneous or foreign 'replacement' gene. This eliminates the need to identify transduced cells by means of selectable markers, greatly simplifying the introduction of foreign genes. Use of fibroblast cells from recipient subjects minimises the possibility of rejection. In addition, culturing the cells in an extracellular matrix circumients the problem of necrosis associated with subcutaneous injection . Clinical diseases which are potential candidates for the gene therapy method include haemophilia, endocrine deficiency, alpha-1-antitrypsin and birth control

L10 ANSWER 11 OF 21 WPIX COPYRIGHT 2009 THOMSON REUTERS on STN
ACCESSION NUMBER: 1992-166882 [20] WPIX
CROSS REFERENCE: 1990-155112; 1992-192207; 1992-414977; 1994-074375; 1993-196268; 1992-276581; 1991-132275; 1992-096256
DOC. NO. CPI: C1992-076692 [21]
TITLE: Prophylaxis and treatment of mast cell implicated diseases - using one or more serine protease inhibitors which bind with mast cell mediators
DERWENT CLASS: B04; D16
INVENTOR: LEZDEY J; WACHTER A; WACHTER A J; WACHTER A M
PATENT ASSIGNEE: (LEZD-I) LEZDEY J; (WACH-I) WACHTER A; (SONO-N) SONORAN DESERT CHEM LLC
COUNTRY COUNT: 38

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 9206706 <--	A1	19920430	(199220)*	EN	22[0] <--	
AU 9189290 <--	A	19920520	(199233)	EN	<--	
EP 512090 <--	A1	19921111	(199246)	EN	0 <--	
US 5190917 <--	A	19930302	(199311)	EN	5[0]	

```
                                                  <--
EP 512090       A4 19930505 (199526)  EN
      <--
                                                  <--
EP 512090       B1 19970102 (199706)  EN  10[0]
      <--
                                                  <--
DE 69123960     E  19970213 (199712)  DE
      <--
                                                  <--
ES 2096665      T3 19970316 (199718)  ES
      <--
                                                  <--
AU 679165       B  19970626 (199734)  EN
      <--
CA 2091354      C  20050412 (200527)  EN
EP 512090       B2 20061122 (200677)  EN
```

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9206706 A1		WO 1991-US6847	19910926
US 5190917 A CIP of		US 1986-946445	19861224
US 5190917 A CIP of		US 1988-181707	19880414
US 5190917 A CIP of		US 1988-242735	19880909
US 5190917 A CIP of		US 1989-445005	19891204
US 5190917 A CIP of		US 1990-591630	19901002
US 5190917 A CIP of		US 1990-598241	19901016
EP 512090 A4		EP 1991-920172	
US 5190917 A		US 1991-683620	19910411
AU 9189290 A		AU 1991-89290	19910926
AU 679165 B		AU 1991-89290	19910926
CA 2091354 C		CA 1991-2091354	19910926
DE 69123960 E		DE 1991-623960	19910926
EP 512090 A1		EP 1991-920172	19910926
EP 512090 B1		EP 1991-920172	19910926
DE 69123960 E		EP 1991-920172	19910926
ES 2096665 T3		EP 1991-920172	19910926
AU 9189290 A		WO 1991-US6847	19910926
EP 512090 A1		WO 1991-US6847	19910926
EP 512090 B1		WO 1991-US6847	19910926
DE 69123960 E		WO 1991-US6847	19910926
CA 2091354 C		WO 1991-US6847	19910926
EP 512090 B2		EP 1991-920172	19910926
EP 512090 B2		WO 1991-US6847	19910926

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
AU 679165	B	Previous Publ	AU 9189290	A
DE 69123960	E	Based on	EP 512090	A
ES 2096665	T3	Based on	EP 512090	A
US 5190917	A	CIP of	US 5008242	A
US 5190917	A	CIP of	US 5114917	A
AU 9189290	A	Based on	WO 9206706	A
EP 512090	A1	Based on	WO 9206706	A
EP 512090	B1	Based on	WO 9206706	A
DE 69123960	E	Based on	WO 9206706	A

AU 679165	B	Based on	WO 9206706	A
CA 2091354	C	Based on	WO 9206706	A
EP 512090	B2	Based on	WO 9206706	A

PRIORITY APPLN. INFO: US 1991-683620 19910411
US 1990-598241 19901016
US 1991-643727 19910118
US 1986-946445 19861224
US 1988-181707 19880414
US 1988-242735 19880909
US 1989-445005 19891204
US 1990-591630 19901002

AN 1992-166882 [20] WPIX

CR 1990-155112; 1992-192207; 1992-414977; 1994-074375; 1993-196268; 1992-276581; 1991-132275; 1992-096256

AB WO 1992006706 A1 UPAB: 20060107
Prevention or direct treatment of mast cell implicated diseases or injury in mammals comprises admin. to the site of disease or injury at least one human serine protease, its analogue, salt or derivative which inhibit the degranulation of mast cells and/or has affinity to mast cell mediators. Inhibitors which may be used are natural or recombinant products selected from alpha 1-antitrypsin, alpha 1-antichymotrypsin, secretory leukocyte protease inhibitor, C-reactive protein, serine amyloid A protein, alpha 2-macroglobulin, eglin, elasnin 3 and elastinal. The serine protease inhibitor inhibits T-cell mediators. The mast cell mediators are neutrophils, basophils or eosinophils or cathepsin G and elastase. Pref. the mast cell implicated disease is a pulmonary inflammation and alpha-1-antitrypsin is administered by inhalation. Treatment with a corticosteroid has a synergistic effect.
USE - Treating inflammatory conditions in patients with mast cell implicated diseases by reducing swelling, pain and stiffness in e.g. skin diseases, e.g. allergic or non-allergic rhinitis incl. rhinitis medicamentosa, rhinitis sicca, atrophic rhinitis and arthritis, burns, atopic dermatitis, bronchial and topical inflammatory conditions, psoriasis, excema and acne. Treatment with a corticosteroid has a synergistic effect. To treat burns a 20% solution of the inhibitor is used

Member(0004)

ABEQ US 5190917 A UPAB 20060107
Treatment of dermatitis or psoriasis comprises topical administration of (a) cpds(s). having affinity to bind and/or inhibit the mediators of most cells and T-cells and (b) 0.1-10 wt.% of a corticosteroid.
(a) Is pref. a serine protease inhibitor, its salt, deriv. or analogue, esp. alpha 1-antitrypsin, alpha 1-antichymotrypsin, secretory leucocyte protease inhibitor, cromolyn C-reactive protein, serum amyloid A protein, alpha 2-macroglobulin, eglin, elastin 3 or elastinal.
(b) Is pref. triamcinoline acetonide, prednisone, hydrocortisone valerate, dexamethasone flurandrenolide or mometasone furoate.
USE - Treatment of dermatitis, psoriasis and other inflammatory skin conditions

L10 ANSWER 12 OF 21 WPIX COPYRIGHT 2009 THOMSON REUTERS on STN
ACCESSION NUMBER: 1992-414977 [50] WPIX
CROSS REFERENCE: 1990-155112; 1991-132275; 1992-096256; 1992-166882; 1992-192207; 1992-276581; 1993-196268; 1994-074375
DOC. NO. CPI: C1992-184164 [21]
TITLE: Treatment of allergic rhinitis - by nasal admin. of serine protease inhibitor
DERWENT CLASS: B04; D16

INVENTOR: LEZDEY J; WACHTER A J
PATENT ASSIGNEE: (LEZD-I) LEZDEY J
COUNTRY COUNT: 1

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 5166134 <--	A	19921124	(199250)*	EN	4[0]	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5166134 A	CIP of	US 1986-946445	19861224
US 5166134 A	CIP of	US 1988-181707	19880414
US 5166134 A	CIP of	US 1989-445005	19891204
US 5166134 A	CIP of	US 1990-591630	19901002
US 5166134 A	CIP of	US 1990-598241	19901016
US 5166134 A		US 1991-710055	19910604

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 5166134 A	CIP of	US 5008242 A

PRIORITY APPLN. INFO: US 1991-710055 19910604
US 1986-946445 19861224
US 1988-181707 19880414
US 1989-445005 19891204
US 1990-591630 19901002
US 1990-598241 19901016

AN 1992-414977 [50] WPIX
CR 1990-155112; 1991-132275; 1992-096256; 1992-166882; 1992-192207; 1992-276581; 1993-196268; 1994-074375
AB US 5166134 A UPAB: 20050701
Allergic rhinitis is treated by nasal administration of at least one serine protease inhibitor or acute phase reactant, its salts, derivs. or analogues, selected from alpha(1)-antitrypsin and alpha(1)-antichymotrypsin.
USE - In the prophylaxis or treatment of allergic rhinitis. This does not limit the inhibitor to the stated cpds.. The inhibitor is one which is capable of binding with a protease in pollen, a protease derived from mast cells, neutrophils or T-cells or of decreasing the degranulation of mast cells. Advantageously the inhibitor binds with a stimulator of IgE synthesis and inhibits mast cell degranulation. The recombinant gene prod. of the invention is especially useful since it is free of contaminating viruses when produced. Pref. the inhibitor is used as an 0.1-2.5wt.% aqueous sol

L10 ANSWER 13 OF 21 WPIX COPYRIGHT 2009 THOMSON REUTERS on STN
ACCESSION NUMBER: 1992-096256 [12] WPIX
CROSS REFERENCE: 1990-155112; 1991-132275; 1992-166882; 1992-192207; 1992-276581; 1992-414977; 1993-196268; 1994-074375
DOC. NO. CPI: C1992-044655 [21]
TITLE: Treatment of pulmonary inflammation - by inhalation of microcrystalline alpha-1-antitrypsin opt. with other serine protease inhibitors
DERWENT CLASS: B04

INVENTOR: LEZDEY J; WACHTER A
PATENT ASSIGNEE: (LEZD-I) LEZDEY J
COUNTRY COUNT: 1

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 5093316	A	19920303	(199212)*	EN	3[0]	

<--

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5093316	A	US 1986-946445	19861224
US 5093316	A	US 1988-181707	19880414
US 5093316	A	US 1988-242735	19880909
US 5093316	A	US 1989-445005	19891204
US 5093316	A	US 1990-591757	19901002

PRIORITY APPLN. INFO: US 1990-591757 19901002
AN 1992-096256 [12] WPIX
CR 1990-155112; 1991-132275; 1992-166882; 1992-192207; 1992-276581; 1992-414977; 1993-196268; 1994-074375
AB US 5093316 A UPAB: 20060106
Inflammatory conditions of the pulmonary tract are treated by administration of monocrystalline alpha-1- antitrypsin or salts or derivatives of this cpd. by inhalation. A compsn. for such treatment comprises the active ingredient and an inert propellant.
ADVANTAGE - Emphysema and alpha-1-anti trypsin deficiencies, resulting in the occurences of the neutrophilis cathepsin G and elastase which cause destruction of the tissue, are currently being treated by injection or infusion of a compsn. containing alpha-1-antitrypsin but such form of administration does not provide rapid relief of the symptoms associated with the disease, particularly inflammation. the present treatment does however, provide this rapid relief. Since alpha-1-antitrypsin only controls elastase it is advisable to utilise other serine prorease inhibitors such as alpha-1-antihymotrypsin C-reactive protein and their mixts. to obtain a broader spectrum of therapy and the present compsns. can also contain such cpds. Asthma may also be controlle

L10 ANSWER 14 OF 21 WPIX COPYRIGHT 2009 THOMSON REUTERS on STN
ACCESSION NUMBER: 1991-353420 [48] WPIX
CROSS REFERENCE: 1988-309289; 1993-085864
DOC. NO. CPI: C1991-152362 [16]
TITLE: Administration of proteinaceous drugs - via aerosol to treat or prevent emphysema
DERWENT CLASS: B04; B07
INVENTOR: CRYSTAL R; ROOSDORP N
PATENT ASSIGNEE: (USSH-C) NAT INST OF HEALTH
COUNTRY COUNT: 1

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 504047	A0	19911022	(199148)*	EN		

<--

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 504047 A0		US 1990-504047	19900403

PRIORITY APPLN. INFO: US 1990-504047 19900403
AN 1991-353420 [48] WPIX
CR 1988-309289; 1993-085864
AB US 7504047 N UPAB: 20050505
The admin. of proteinaceous therapeutic prods. in the form of an aerosol in treating or preventing disease states of the lung is disclosed. The protein is especially a recombinant alpha1-aniotrypsin to inhibit elastase.
USE/ADVANTAGE - The aerosol formulations provide a physiologically effective dosage in the lungs to treat or prevent emphysema. Other cpds. may also be delivered to treat pathogenic infections e.g. viruses, protists, or prokaryotes and other diseases treated are asthma, adult or infant respiratory distress syndrome and lung cancer. Dosage is 0.1-15, pref. 0.5-10 wt% aerosol agent. Dosage of alpha1-antitrypsin is 1 microg-10 mg/kg host, and the period of admin. is 2 sec. - 30 mins., pref. 3-7 sec. with metered dose inhales and 10-20 mins. for rebulisers. Admin. may be a single dosage or more within 2-24 hrs.. The drugs are retained in the lung epithelial lining fluid to maintain an effective concentration in the lung in contact with lung tissue for extended periods of time.

L10 ANSWER 15 OF 21 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1990299848 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2113921
TITLE: Trypsin inhibitors in guinea pig plasma: isolation and characterization of contrapsin and two isoforms of alpha-1-antiproteinase and acute phase response of four major trypsin inhibitors.
AUTHOR: Suzuki Y; Yoshida K; Ichimiya T; Yamamoto T; Sinohara H
CORPORATE SOURCE: Department of Biochemistry, Kinki University School of Medicine, Osaka.
SOURCE: Journal of biochemistry, (1990 Feb) Vol. 107, No. 2, pp. 173-9.
Journal code: 0376600. ISSN: 0021-924X.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199008
ENTRY DATE: Entered STN: 7 Sep 1990
Last Updated on STN: 3 Mar 2000
Entered Medline: 6 Aug 1990
AB Contrapsin and two isoforms, F (fast) and S (slow), of alpha-1-antiproteinase (also called alpha-1-proteinase inhibitor) were isolated in an apparently homogeneous state from plasma of inflamed guinea pigs. Contrapsin inactivated trypsin, but did not significantly affect chymotrypsin, pancreatic elastase, or pancreatic kallikrein. On the other hand, both isoforms of alpha-1-antiproteinase inhibited trypsin, chymotrypsin, and elastase, but not plasma or pancreatic kallikrein. The S isoform of alpha-1-antiproteinase was present in barely detectable amounts in healthy animals, but increased markedly when the acute-phase reaction was induced by subcutaneous injection of turpentine. On the other hand, the plasma levels of the F isoform, contrapsin, and alpha-macroglobulin showed moderate (1.5 to 2.3-fold) elevation during the acute-

phase reaction. In contrast to the previous findings that rats and rabbits contain two different alpha-macroglobulins, one of which is an acute-phase reactant while the other is not, inflamed guinea pigs contained only one species of alpha-macroglobulin. Murinoglobulin, the most prominent acute-phase negative protein in both mice and rats, showed no significant change in guinea pigs. These results indicate that guinea pig plasma contains four major trypsin inhibitors, i.e., contrapsin, alpha-1-antiproteinase, alpha-macroglobulin, and murinoglobulin, the properties of which are very similar to those of the respective mouse homologues, but that the acute-phase response of these inhibitors differs greatly from that of the homologous proteins in rats or mice.

L10 ANSWER 16 OF 21 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 1989382092 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2778627
TITLE: Effect of acute-phase proteinase inhibitors on chemotaxis of rat polymorphonuclear leukocytes in vitro.
AUTHOR: Nakagawa H; Sato K; Miyai H; Yamamoto Y
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Toyama Medical and Pharmaceutical University, Japan.
SOURCE: Journal of pharmacobio-dynamics, (1989 Jun) Vol. 12, No. 6, pp. 363-9.
Journal code: 7901854. ISSN: 0386-846X.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198910
ENTRY DATE: Entered STN: 9 Mar 1990
Last Updated on STN: 9 Mar 1990
Entered Medline: 19 Oct 1989

AB Rat serum obtained at 24 h after subcutaneous injection of carrageenin significantly suppressed chemotaxis of rat polymorphonuclear leukocytes (PMNs) in vitro. alpha 2 Acute-phase macroglobulin (alpha 2APM), alpha 1 proteinase inhibitor (alpha 1 PI) and cysteine-proteinase inhibitors (CPIs) are present at high concentration in the 24-h serum and known as acute-phase reactants in rats. These acute-phase proteinase inhibitors were purified from inflamed rat serum or exudate and their effect on PMN chemotaxis was studied by Boyden's method in vitro. alpha 2 APM (4 mg/ml) significantly suppressed PMN chemotaxis while alpha 1M was without effect, though both alpha 2APM and alpha 1M had a similar anti-proteinase activity. The results suggest that alpha 2APM suppressed PMN chemotaxis through the mechanism unrelated to its anti-proteinase activity. On the other hand, alpha 1PI (1 and 3 mg/ml) slightly but significantly suppressed PMN chemotaxis, whereas CPI-1 and CPI-2 had no inhibitory effect. These results suggest that alpha 2APM and alpha 1PI play a role in suppression of PMNs infiltration into the inflammatory site in the late-phase of acute inflammation.

L10 ANSWER 17 OF 21 MEDLINE on STN
ACCESSION NUMBER: 1989353591 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2788479
TITLE: [Levels of alpha 1-antitrypsin in the blood of patients with chronic bronchitis].
Hladiny alfa 1-antitrypsinu v sere chorych na chronicku

bronchitidu.
AUTHOR: Hal'ak O; Pullmann R; Jamriska P; Rozborilova E; Chalupova E; Kavcova E; Hazlingerova M
SOURCE: Bratislavske lekarske listy, (1989 Apr) Vol. 90, No. 4, pp. 290-3.
Journal code: 0065324. ISSN: 0006-9248.
PUB. COUNTRY: Czechoslovakia
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Slovak
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198909
ENTRY DATE: Entered STN: 9 Mar 1990
Last Updated on STN: 9 Mar 1990
Entered Medline: 28 Sep 1989

AB Serum levels of alpha 1-antitrypsin were studied in 80 patients with chronic bronchitis. As a manifestation of the inflammatory response, nonsignificant increase was recorded compared to the group of healthy subjects. In discordance with literary data, no significant differences were found between bronchitics smokers and non-smokers. In 5 patients (6.2%), alpha 1-antitrypsin serum levels were below the lower limit of the reference range. The patients complained of cough, expectoration, and dyspnea. As a preventive measure, it is recommended to determine serum alpha 1- antitrypsin levels in smokers before they take up a job in a dusty environment and in bronchitics before inhalation treatment with proteolytic enzymes is administered. In alpha 1-antitrypsin deficit the value of substitution therapy in patients with emphysema is being emphasized.

L10 ANSWER 18 OF 21 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 1989214017 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2468654
TITLE: Acute phase response of plasma proteins in analbuminemic rats.
AUTHOR: Goto K; Saito A; Nagase S; Sinohara H
CORPORATE SOURCE: Department of Biochemistry, Kinki University School of Medicine, Osaka.
SOURCE: Journal of biochemistry, (1988 Dec) Vol. 104, No. 6, pp. 952-5.
Journal code: 0376600. ISSN: 0021-924X.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198905
ENTRY DATE: Entered STN: 6 Mar 1990
Last Updated on STN: 29 Jan 1996
Entered Medline: 26 May 1989

AB In healthy Nagase analbuminemic rats (NAR), the highest degree of relative increase in serum protein concentration was found for alpha-2-macroglobulin, the most prominent acute phase protein in rats. Its levels were about 30- and 60-fold higher in males and females, respectively, than those in the control Sprague-Dawley (SD) rats. In terms of absolute concentration, however, alpha-1-inhibitor 3 (also called alpha-X-protein or murinoglobulin) showed the most conspicuous change, its levels being higher by about 7 mg/ml than those in SD. When the acute phase reaction was induced by subcutaneous injection of turpentine, the levels of alpha-1- and alpha-2-macroglobulins, alpha-1-cysteine proteinase inhibitor, alpha-1-antiproteinase , and alpha-1-inhibitor 3 in NAR changed in essentially the same way as in SD: alpha-1-inhibitor 3 decreased markedly while the rest increased further.

These results suggest that mechanisms responsible for the elevation of serum globulins in healthy NAR are not directly related to those involved in the acute phase response. On the other hand, the antithrombin III levels in healthy NAR were about twice the control values and changed little during the inflammation. In contrast, this protein in SD doubled during the acute phase, its maximal levels being close to those in healthy or inflamed NAR. This suggests that the antithrombin III level in healthy NAR is regulated by a mechanism similar to that in SD maximally reacting to the acute phase stress.(ABSTRACT TRUNCATED AT 250 WORDS)

L10 ANSWER 19 OF 21 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 1988235354 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2453907
TITLE: Bovine acute phase response following turpentine injection.
AUTHOR: Conner J G; Eckersall P D; Wiseman A; Aitchison T C; Douglas T A
CORPORATE SOURCE: Department of Clinical Biochemistry, University of Glasgow Veterinary School.
SOURCE: Research in veterinary science, {1988 Jan} Vol. 44, No. 1, pp. 82-8.
Journal code: 0401300. ISSN: 0034-5288.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198806
ENTRY DATE: Entered STN: 8 Mar 1990
Last Updated on STN: 8 Mar 1990
Entered Medline: 24 Jun 1988
AB The serum levels of five proteins, alpha 1 antitrypsin, ceruloplasmin, fibrinogen, haptoglobin and seromucoid, were measured daily in calves after the subcutaneous injection of oil of turpentine. Raised concentrations were detected on the second and third days after injection with peak levels occurring on the fourth to seventh days and returning to normal by the 17th day. Levels of four of these proteins, alpha 1 antitrypsin, ceruloplasmin, haptoglobin and seromucoid were compared in the same calves following three different doses of turpentine. Levels of haptoglobin and seromucoid varied with the dose whereas ceruloplasmin and alpha 1 antitrypsin levels did not.

L10 ANSWER 20 OF 21 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 1985224194 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2408567
TITLE: Plasma protein and liver mRNA levels of two closely related murine alpha 1-protease inhibitors during the acute phase reaction.
AUTHOR: Frazer J M; Nathoo S A; Katz J; Genetta T L; Finlay T H
SOURCE: Archives of biochemistry and biophysics, {1985 May 15} Vol. 239, No. 1, pp. 112-9.
Journal code: 0372430. ISSN: 0003-9861.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198506

ENTRY DATE: Entered STN: 20 Mar 1990
Last Updated on STN: 20 Mar 1990
Entered Medline: 24 Jun 1985

AB Plasma levels of alpha 1-PI(T) and alpha 1-PI(E), two closely related murine alpha 1-protease inhibitors, having affinities for trypsin and elastase, respectively, were compared to changes in specific liver mRNA levels after induction of the acute-phase reaction by subcutaneous injection of turpentine. In earlier, qualitative experiments an increase in plasma levels of alpha 1-PI(E), but not alpha 1-PI(T), during the acute-phase reaction had been shown. It is now shown that stimulation of plasma alpha 1-PI(E) levels reaches a maximum of 35-50% above baseline 12 h after induction of the acute-phase response using either a functional or immunological assay to measure protease inhibitor activity. Consistent with earlier observations, little or no change in plasma levels of alpha 1-PI(T) is seen. Determination of mRNA levels in the mouse liver specific for alpha 1-PI(E) and alpha 1-PI(T) was accomplished using a cell-free translation system followed by immunoprecipitation of the 35S-labeled protease inhibitors. The apparent Mr's of alpha 1-PI(E) and alpha 1-PI(T) synthesized in vitro are 42K and 46K, respectively. Apparent Mr's of the native proteins in plasma are 55K and 65K. Unexpectedly, mRNA levels for both alpha 1-PI(E) and alpha 1-PI(T) were found to increase after induction of the acute-phase reaction. Maximal stimulation for both mRNAs was approximately 300% and occurred 9 h after turpentine administration. Under these conditions, levels of translatable albumin mRNA in the mouse liver decreased to 40% of baseline in 6-9 h.

L10 ANSWER 21 OF 21 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 1933:13034 BIOSIS Full-text
DOCUMENT NUMBER: PREV19330700013088; BA07:13088
TITLE: The protection of insulin by antiproteases, and its absorption from the intestine.
AUTHOR(S): HARNED, BEN K.; NASH, THOMAS P.
SOURCE: JOUR BIOL CHEM, (1932) Vol. 97, No. 2, pp. 443-456.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: Unavailable
ENTRY DATE: Entered STN: May 2007
Last Updated on STN: May 2007

AB A preparation of antitrypsin is described which is at least 90% effective in preventing inactivation of insulin by pancreatin under in vitro conditions favorable for tryptic digestion. Apparently a stoichiometric relation holds between trypsin and antitrypsin, since a small amount of antitrypsin will not afford protection against an indefinitely large amount of trypsin. The unique advantages of insulin as an indicator of anti-enzyme effectiveness are cited. No insulin effects can be observed in the normal dog when mixtures of insulin and antitrypsin are introduced directly into the duodenum, perhaps because of a compensatory decrease in insulin secretion by the pancreas. Insulin administered by stomach tube to depancreatized dogs has no effect upon sugar excretion or D:N ratios. When mixed with antitrypsin and given by stomach tube, insulin causes a marked decrease in sugar output, thus indicating an antipeptic activity of the anti- trypsin preparation. Insulin alone or with antitrypsin, introduced directly into the duodenum of the depancreatized dog, will abolish the sugar excretion for short periods and maintain the urine sugar values at low levels for longer periods. Compensatory, high D:N ratios in subsequent periods suggest an interim storage of glycogen. Subcutaneous injection of antitrypsin alone in rabbits and subcutaneous or enteral administration in dogs have no detectable effect upon blood or urine sugar.

The relatively small absorption of insulin direct from the intestine, and the failure of our antiprotease mixture to improve its absorption, are probably attributable either to inactivation of the major portion by intestinal enzymes or bacteria, or to inherent physical obstacles to diffusion imposed by the protein character of insulin. ABSTRACT AUTHORS: Authors' summary

```
            (FILE 'HCAPLUS' ENTERED AT 14:15:43 ON 18 MAY 2009)
L1           20 SEA FILE=REGISTRY ABB=ON  PLU=ON  "A1-ANTITRYPSIN"?/CN
L2        10337 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 OR (A1 OR ALPHA1 OR
                (ALPHA OR A)(1A)1)(A)(ANTITRYPSIN OR ANTI(W)(TRYPSIN OR
                PROTEINASE OR PROTEASE) OR ANTIPROTEASE OR ANTIPROTEINASE
                OR (PROTEASE OR PROTEINASE)(W)INHIBIT?) OR A1PI OR
                PROLASTIN OR ZEMAIRA OR AAT(10A)?TRYPSIN? OR A1AT OR
                ANTITRYPSIN OR ANTI TRYPSIN
L3          392 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L2(30A)(ADMIN? OR INJECT?
                OR APPLY? OR APPLIED OR APPLICATION)
L4           73 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3(30A)(PARENTAL? OR
                ORAL? OR MOUTH OR VAGINAL? OR RECTAL? OR ANAL OR NASAL? OR
                MOSE OR BUCCAL? OR INTRAVENOUS? OR IV OR I V OR INTRA(W)(VE
                NOUS? OR MUSCUL? OR CEREBROVENTRIC?) OR INTRAMUSCUL? OR
                SUBCUTANEOUS? OR INTRATHECAL? OR EPIDURAL? OR TRANSDERMAL?
                OR INTRACEREBROVENTRIC?)
L5            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3(30A)(OSMOTIC?(W)PUMP
                OR INHALE# OR INHALANT OR INHALING OR INHALATION?)
L6           46 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L4 OR L5) AND (PY<2000
                OR AY<2000 OR PRY<2000)


L11          37 S L6 NOT L8
```

L11 ANSWER 1 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN

ED Entered STN:	07 Dec 2000
ACCESSION NUMBER:	2000:855756 HCAPLUS Full-text
DOCUMENT NUMBER:	134:32965
TITLE:	Polypeptide composition for oral administration
INVENTOR(S):	Grass, George M.; Sweetana, Stephanie A.
PATENT ASSIGNEE(S):	G.D. Searle and Co., USA
SOURCE:	U.S., 15 pp., Cont. of U.S. Ser. No. 350,067, abandoned. CODEN: USXXAM
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6156731	A	20001205	US 1995-567501 <--	19951205
PRIORITY APPLN. INFO.:			US 1989-350067 <--	B1 19890510

AB There is disclosed a composition containing a biol. active polypeptide selected from LHRH, an LHRH analog, somatostatin and a somatostatin analog, in a therapeutically effective amount, a membrane permeability enhancing agent, and a protease enzyme inhibitor enveloped within an enteric coating. The composition possesses enhanced bioavailability upon oral administration. A formulation was prepared containing Na glycocholate, aprotinin, and RS-94991-268 (nafarelin acetate), propylene glycol, and sorbitol for filling capsules.

IT 9041-92-3, α1-Antitrypsin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(polypeptide composition for oral administration)
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 14 Feb 1998
ACCESSION NUMBER: 1998:86265 HCAPLUS Full-text
DOCUMENT NUMBER: 128:163356
ORIGINAL REFERENCE NO.: 128:32059a,32062a
TITLE: Genomic DNA transfer with a high-capacity adenovirus vector results in improved in vivo gene expression and decreased toxicity
AUTHOR(S): Schiedner, Gudrun; Morral, Nuria; Parks, Robin J.; Wu, Ying; Koopmans, Suzanne C.; Langston, Claire; Graham, Frank L.; Beaudet, Arthur L.; Kochanek, Stefan
CORPORATE SOURCE: Dep. Mol. and Human Genetics, Baylor Coll. Med., Houston, TX, 77030, USA
SOURCE: Nature Genetics (1998), 18(2), 180-183
CODEN: NGENEC; ISSN: 1061-4036
PUBLISHER: Nature America
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Many applications for human gene therapy would be facilitated by high levels and long duration of physiol. gene expression. Adenoviral vectors are frequently used for gene transfer because of their high cellular transduction efficiency in vitro and in vivo. Expression of viral proteins and the low capacity for foreign DNA limits the clin. application of first- and second generation adenoviral vectors. Adenoviral vectors with all viral coding sequences deleted offer the prospect of decreased host immune responses to viral proteins, decreased cellular toxicity of viral proteins and increased capacity to accommodate large regulatory DNA regions. Currently most vectors used in vivo for preclin. and clin. studies express cDNAs under the control of heterologous eukaryotic or viral promoters. Using an adenoviral vector with all viral coding sequences deleted and containing the complete human .alpha.1-antitrypsin (PI)locus, we observed tissue-specific transcriptional regulation in cell culture and in vivo; i.v. injection in mice resulted in high levels of very stable expression for more than ten months and decreased acute and chronic toxicity. These results indicate significant advantages of regulated gene expression using genomic DNA for gene transfer and of adenoviral gene transfer vector devoid of all viral coding sequences.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 17 Nov 1997
ACCESSION NUMBER: 1997:724428 HCAPLUS Full-text
DOCUMENT NUMBER: 128:2563
ORIGINAL REFERENCE NO.: 128:567a,570a
TITLE: Investigation of the presence of apolipoprotein E, glycosaminoglycans, basement membrane proteins, and protease inhibitors in senile interstitial amyloid of the pituitary
AUTHOR(S): Rocken, Christroph; Paris, Diana; Steusloff, Karen; Saeger, Wolfgang
CORPORATE SOURCE: Marienkrankenhaus, Institute of Pathology, Hamburg, Germany
SOURCE: Endocrine Pathology (1997), 8(3),

205-214
CODEN: ENPAFD; ISSN: 1046-3976
PUBLISHER: Humana
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim of the authors' study was to test whether local- or organ-limited interstitial amyloid of the pituitary is associated with the presence of glycosaminoglycans, basement membrane proteins, protease inhibitors, and apolipoprotein E (apo e), as previously observed in other amyloid syndromes. Serial sections from amyloidotic and nonamyloidotic autopsy pituitaries of patients age 85 yr and over were stained with Congo red, Alcian blue, and applying immunohistochem., with antibodies directed against fibronectin, collagen IV, laminin, apo E, .alpha.1- antitrypsin and α1-antichymotrypsin. Interstitial amyloid was deposited in the immediate vicinity of capillaries and around the acini of the anterior lobe. Glycosaminoglycans were found in capillaries and around the acini of both nonamyloidotic and amyloidotic glands and they were also related spatially to amyloid deposits. Immunostaining of nonamyloidotic and amyloidotic glands demonstrated the presence of fibronectin, collagen IV, and laminin, which was related to basement membranes (fibronectin, collagen IV, and laminin), interstitium, and serum (fibronectin only). In amyloidotic glands, each basement membrane protein presented with an addnl. spatial relation to amyloid deposits. Apo E was found in amyloidotic cases only within the amyloid deposits. The results are consistent with the presence of glycosaminoglycans, basement membrane proteins, and apo E in local interstitial amyloid deposits of the pituitary, as previously described in other amyloid syndromes, such as inflammatory related AA-amyloidosis or Aβ-amyloidosis related to Alzheimer's disease.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN

ED Entered STN: 22 Oct 1997
ACCESSION NUMBER: 1997:669460 HCAPLUS Full-text
DOCUMENT NUMBER: 127:302895
ORIGINAL REFERENCE NO.: 127:59039a,59042a
TITLE: Pharmacokinetic study of α1-antitrypsin infusion in α1-antitrypsin deficiency
AUTHOR(S): Barker, Alan F.; Iwata-Morgan, Irene; Oveson, Lynn; Roussel, Ralph
CORPORATE SOURCE: Department of Medicine, Oregon Health Sciences University, Portland, USA
SOURCE: Chest (1997), 112(3), 607-613
CODEN: CHETBF; ISSN: 0012-3692
PUBLISHER: American College of Chest Physicians
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To ascertain how long 120 mg/kg alpha1-antitrypsin concentrate (α1-AT-C), administered IV every 2 wk, can maintain .alpha.1-antitrypsin (. alpha.1-AT) serum levels above 70 to 80 mg/dL. Secondary objectives were to summarize the nature, severity, and relationship of a plasma-derived α1-AT-C infusion to any side effects. This was an open-label uncontrolled pharmacokinetic study. α1-AT-C was administered IV every 2 wk for 10 infusions in 23 patients with PIZ α1-AT deficiency. Serum α1-AT levels and neutralizing elastase activity were measured preinfusion, postinfusion, and at nadir. During two infusion periods, daily serum α1-AT and neutralizing elastase activities were measured on the seventh to 14th days. Five patients received BAL assays for α1-AT and neutralizing elastase activity. Adverse events were recorded in a patient

diary and by a nurse at each infusion visit. The 120-mg/kg dose of α1-AT-C could not maintain nadir serum protective levels above 70 or 80 mg/dL for the entire 14-day dosing interval in most patients. None of the patients had α1-AT levels above 80 mg/dL for all 14 days. The serum α1-AT and neutralizing elastase levels correlated suggesting functional activity. The BAL α1-AT and neutralizing elastase activities were low and did not correlate with serum levels. α1-AT-C at 120 mg/kg administered every 2 wk did not maintain nadir serum α1-AT levels above 70 to 80 mg/dL for a 14-day dosing interval. Higher doses every 2 wk or decreased interval between infusions may be required.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 25 Sep 1996
ACCESSION NUMBER: 1996:571014 HCAPLUS Full-text
DOCUMENT NUMBER: 125:239611
ORIGINAL REFERENCE NO.: 125:44585a,44588a
TITLE: Development of a complementing cell line and a system for construction of adenovirus vectors with E1 and E2a deleted
AUTHOR(S): Zhou, Heshan; O'Neal, Wanda; Morral, Nuria; Beaudet, Arthur L.
CORPORATE SOURCE: Department Molecular Human Genetics, Baylor College Medicine, Houston, TX, 77030, USA
SOURCE: Journal of Virology (1996), 70(10), 7030-7038
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Although adenovirus vectors offer many advantages, it would be desirable to develop vectors with improved expression and decreased toxicity. Toward this objective, an adenovirus vector system with deletion of both the E1 and E1a regions was developed. A 5.9-kb fragment of the adenovirus type 5 (Ad5) genome containing the E2a gene and its early and late promoters was transfected into 293 cells. A complementing cell line, designated 293-C2, expressed the E2a mRNA and protein and was found to complement the defect in Ad5 viruses with temperature-sensitive or deletion mutations in E2a. A deletion of 1.3 kb removing condons 40 to 471 of the 529 amino acids of E2a was introduced into plasmids for preparation of viruses and vectors. An Ad5 virus with disruption of the E1 gene and deletion of E2a grew on 293-C2 cells but not on 293 cells. Vectors with E1 and E2a deleted expressing Escherichia coli β-galactosidase or human . alpha.1-antitrypsin were prepared and expressed the reporter genes after i.v. injection into mice. This vector system retains sequences in common between the complementing cell line and the vectors, including 3.4 kb upstream and 1.1 kb downstream of the deletion. These vectors have potential advantages of increased capacity for insertion of transgene sequences, elimination of expression of E2a, and possibly reduction in expression of other viral proteins. Although the titers of the vectors with deleted are about 10- to 30-fold below those of vectors with E2a wild-type regions, the former vectors are suitable for detailed studies with animals to evaluate the effects on host immune responses and on duration of expression.

L11 ANSWER 6 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 18 Jun 1996
ACCESSION NUMBER: 1996:351212 HCAPLUS Full-text

DOCUMENT NUMBER: 125:75682
ORIGINAL REFERENCE NO.: 125:14134h,14135a
TITLE: Parameters of serological effects following oral administration of Mulsal N: Results of a double-blind study
AUTHOR(S): Kunze, R.
CORPORATE SOURCE: IMTOX GmbH, Berlin, D-13355, Germany
SOURCE: Absorption of Orally Administered Enzymes (1995), 69-75. Editor(s): Gardner, Michael L. G.; Steffens, Klaus-Juergen. Springer: Berlin, Germany.
CODEN: 62XRAI
DOCUMENT TYPE: Conference
LANGUAGE: English

AB A double-blind study was performed to study the effects of Mulsal N. The blood levels of α1-antitrypsin, α2-macroglobulin, C-reactive protein and fibrinogen were assessed following administration of Mulsal N. The results confirm that oral Mulsal N has a pos. effect on these inflammatory serum parameters.

IT 9041-92-3, α1-Antitrypsin
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(parameters of serol. effects following oral administration of Mulsal N)

L11 ANSWER 7 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 17 Feb 1996
ACCESSION NUMBER: 1996:99539 HCAPLUS Full-text
DOCUMENT NUMBER: 124:139759
ORIGINAL REFERENCE NO.: 124:25843a,25846a
TITLE: Process for separating alpha1-antitrypsin from Cohn fraction IV1 and IV4 paste
INVENTOR(S): Taniguchi, Tom; Rolf, John M.; Bhattacharya, Prabir; Uemura, Yahiro
PATENT ASSIGNEE(S): Alpha Therapeutic Corp., USA
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9535306	A1	19951228	WO 1995-US7616 <--	19950616
W: CA, JP RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6284874	B1	20010904	US 1994-261406 <--	19940617
PRIORITY APPLN. INFO.:			US 1994-261406 A <--	19940617

AB The present invention is directed to a process for purifying α1-proteinase inhibitor. The process comprises providing an impure protein fraction which comprises α1-proteinase inhibitor. The impure protein fraction is precipitated with a precipitant comprising PEG. The supernatant from the PEG precipitation, which comprises α1-proteinase inhibitor, is collected and applied to an anion-exchange medium. A fraction comprising α1-proteinase inhibitor is recovered from the anion-exchange medium and applied to a metal

chelate medium. A fraction comprising α1-proteinase inhibitor is then recovered from the metal chelate medium. Alpha1-proteinase inhibitor purified by the process has a specific activity greater than 0.6 units/mg. .alpha.1-Antitrypsin prepared as described was nontoxic to rabbits when administered i.v. at a dose of 240 mg/kg body weight

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 14 Nov 1995
ACCESSION NUMBER: 1995:915135 HCAPLUS Full-text
DOCUMENT NUMBER: 123:350080
ORIGINAL REFERENCE NO.: 123:62617a,62620a
TITLE: Pharmacokinetics of a Novel HIV-1 Protease Inhibitor Incorporated into Biodegradable or Enteric Nanoparticles following Intravenous and Oral Administration to Mice
AUTHOR(S): Leroux, Jean-Christophe; Cozens, Robert; Roesel, Johan L.; Galli, Bruno; Kubel, Frank; Doelker, Eric; Gurny, Robert
CORPORATE SOURCE: School of Pharmacy, University of Geneva, Geneva, CH-1211, Switz.
SOURCE: Journal of Pharmaceutical Sciences (1995), 84(12), 1387-91
CODEN: JPMSAE; ISSN: 0022-3549
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CGP 57813 is a peptidomimetic inhibitor of human immunodeficiency virus type 1 (HIV-1) protease. This lipophilic compound was successfully entrapped into poly(D,L-lactic acid) (PLA) and pH sensitive methacrylic acid copolymers nanoparticles. The i.v. administration to mice of PLA nanoparticles loaded with CGP 57813 resulted in a 2-fold increase of the area under the plasma concentration-time curve, compared to a control solution An increase in the elimination half-life (from 13 to 61 min) and in the apparent volume of distribution (1.7-3.6 L/kg) was observed for the nanoparticle incorporated compound vs control solution Following oral administration, only nanoparticles made of the methacrylic acid copolymer soluble at low pH provided sufficient plasma levels of CGP 57813. In vitro, these nanoparticles dissolved completely within 5 min at pH 5.6. PLA nanoparticles, which are insol. in the gastrointestinal tract, did not provide significant plasma concns. of CGP 57813. From these observations, one can conclude that the passage of intact PLA nanoparticles across the gastrointestinal mucosa appears to be very low.

L11 ANSWER 9 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 23 Nov 1994
ACCESSION NUMBER: 1995:209340 HCAPLUS Full-text
DOCUMENT NUMBER: 122:47818
ORIGINAL REFERENCE NO.: 122:9049a,9052a
TITLE: Expression of human α1-antitrypsin in mouse after in vivo gene transfer to hepatocytes by small liposomes
AUTHOR(S): Alino, S. F.; Crespo, J.; Bobadilla, M.; Lejarreta, M.; Blaya, C.; Crespo, A.
CORPORATE SOURCE: Fac. Med. Dentistry, Univ. Valencia, Valencia, 46010, Spain
SOURCE: Biochemical and Biophysical Research

Communications (1994), 204(3), 1023-30
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A plasmid (pTG7101) containing the full-length human α 1-antitrypsin gene was encapsulated in small liposomes and used for "in vivo" gene transfer to mouse hepatocytes, by i.v. injection (100 ng DNA/mouse and dose). The expression of human protein was evaluated by microspectrophotometry after human α1-antitrypsin immunoperoxidase reaction on liver cryosections and the presence in mouse plasma of de novo synthesized protein was detected by ELISA anal. The results indicate that a single dose of encapsulated plasmid induces the expression of human α1-antitrypsin in mouse hepatocytes and a large effect (70%) remains two weeks after treatment. However, no effect was observed when mice were treated with buffer or free plasmid (100 ng/mouse) plus an equivalent lipid dose of empty liposomes. In addition, whereas no additive effect was observed after repetitive treatment-doses, the partial hepatectomy three hours after a single treatment-dose, significantly increased the presence of human α1-antitrypsin in mice plasma.

L11 ANSWER 10 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 12 Nov 1994
ACCESSION NUMBER: 1994:621901 HCAPLUS Full-text
DOCUMENT NUMBER: 121:221901
ORIGINAL REFERENCE NO.: 121:40165a,40168a
TITLE: No lung toxicity after repeated aerosol or intravenous delivery of plasmid-cationic liposome complexes
AUTHOR(S): Canonico, Angelo E.; Plitman, Jonathan D.; Conary, Jon T.; Meyrick, Barbara O.; Brigham, Kenneth L.
CORPORATE SOURCE: School of Medicine, Vanderbilt University, Nashville, TN, 37232, USA
SOURCE: Journal of Applied Physiology (1994), 77(1), 415-19
CODEN: JAPHEV; ISSN: 8750-7587
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The safety aspects of human gene therapy are of paramount importance in developing an ideal system for gene transfer. Lipofection using DNA in the form of a plasmid has been shown to successfully transfect the lungs when administered either i.v. or by aerosol. The authors have shown that repeated i.v. or aerosol administration of a plasmid containing the recombinant human . alpha.1-antitrypsin gene and a cytomegalovirus promoter complexed to cationic liposomes results in no adverse effects on pulmonary histol., lung compliance, lung resistance, or alveolar-arterial oxygen gradient. Immunohistochem. and Western blot anal. confirm successful gene transfer using this delivery system. The authors conclude that plasmids complexed to cationic liposomes may be a safe and efficacious delivery system for in vivo gene transfer to the lungs. Using this delivery system, in vivo gene therapy to the lungs can be achieved by either i.v. or aerosol administration of the transgene.

L11 ANSWER 11 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 12 Jun 1993
ACCESSION NUMBER: 1993:226825 HCAPLUS Full-text
DOCUMENT NUMBER: 118:226825
ORIGINAL REFERENCE NO.: 118:39019a,39022a

TITLE: In vivo delivery of human α 1-antitrypsin gene to mouse hepatocytes by liposomes
AUTHOR(S): Alino, S. F.; Bobadilla, M.; Garcia-Sanz, M.; Lejarreta, M.; Unda, F.; Hilario, E.
CORPORATE SOURCE: Fac. Med. Dent., Univ. Valencia, Valencia, 46010, Spain
SOURCE: Biochemical and Biophysical Research Communications (1993), 192(1), 174-81
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The pTG7101 plasmid containing the full-length human α 1-antitrypsin gene was encapsulated in large (142±15 nm of diameter) and small (54±11 nm of diameter) liposomes and administered i.v. to mice (80 ng/mouse). Control animals were treated with empty (small and large) liposomes plus free DNA and with the liposome solvent buffer. The immunohistochem. results on liver criosections and cytophotometric anal. of hepatocyte chromophore absorbance, after peroxidase reaction, indicated that significant presence of immunoreactive human α 1-antitrypsin was present 7 days after treatment of mice with encapsulated DNA in small liposomes but not when large liposomes were used. This effect was observed in a great number of liver parenchymal cells. These results agree with the observation that only small liposomes have easy access to hepatocytes and support the idea that small liposomes are appropriate vehicles for in vivo delivery of specific genetic material to liver parenchymal cells, with high efficiency.

L11 ANSWER 12 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 08 Dec 1990
ACCESSION NUMBER: 1990:609753 HCAPLUS Full-text
DOCUMENT NUMBER: 113:209753
ORIGINAL REFERENCE NO.: 113:35437a,35440a
TITLE: In vivo evidence for protease-catalyzed mechanism providing bioactive tumor necrosis factor α
AUTHOR(S): Niehoerster, Marcus; Tiegs, Gisa; Schade, Ulrich F.; Wendel, Albrecht
CORPORATE SOURCE: Fac. Biol., Univ. Konstanz, Konstanz, D-7750, Germany
SOURCE: Biochemical Pharmacology (1990), 40(7), 1601-3
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mice pretreated by i.v. injection of the serine protease inhibitor α 1-antitrypsin prior to a hepatotoxic dose of D-galactosamine/lipopolysaccharide (GalN/LPS) were fully protected against hepatitis. Pretreatment with α1-antitrypsin with doses up to 300 mg/kg at different times failed to protect galactosamine sensitized animals against tumor necrosis factor α (TNFα)-induced hepatitis. No bioactive TNFα was detectable in serum of mice protected against GalN/LPS-induced hepatitis by pretreatment with α1-antitrypsin. In contrast, abundant amts. of TNF were found in sera of GalN/LPS-treated control animals. Thus, a serine protease sensitive to α1-antitrypsin provides bioactive TNFα by proteolytic cleavage of a TNFα precursor.

L11 ANSWER 13 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 01 Oct 1988

ACCESSION NUMBER: 1988:509239 HCAPLUS Full-text
DOCUMENT NUMBER: 109:109239
ORIGINAL REFERENCE NO.: 109:18189a,18192a
TITLE: Investigation of the effects of oral administration of ascorbate on the functional activity of serum α-1-protease inhibitor and oxidant release by blood phagocytes from cigarette smokers in a placebo-controlled, doubleblind, crossover trial
AUTHOR(S): Theron, A. J.; Anderson, R.
CORPORATE SOURCE: Inst. Pathol., Univ. Pretoria, Pretoria, S. Afr.
SOURCE: International Journal for Vitamin and Nutrition Research (1988), 58(2), 218-24
CODEN: IJVNAP; ISSN: 0300-9831
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of oral administration of ascorbate (3 g daily for 14 days) on the elastase inhibitory capacity (EIC) of serum α-1-protease inhibitor (API) and on the profile of leukoattractant (FMLP)-activated luminol-enhanced chemiluminescence (LECL) responses of blood from 29 cigaret smokers were investigated in a placebo-controlled, double-blind crossover trial. Relative to nonsmokers, the EIC's of serum API from cigaret smokers showed no detectable functional inactivation. However the blood LECL responses were significantly greater in smokers than in nonsmokers. Serum EIC activity remained unchanged during the administration of ascorbate to cigaret smokers. However the early-occurring extracellular LECL responses of FMLP-activated blood from cigaret smokers declined significantly during intake of ascorbate by the 29 cigaret smokers. These inhibitory effects of ascorbate on the extracellular LECL responses were highly significant in smokers (15/29) with elevated (1 + SD higher than the mean value for nonsmokers) extracellular LECL responses, whereas the corresponding values in smokers with normal LECL responses remained unchanged during ascorbate administration. These results show that measurement of serum EIC capacity in the setting of normal API levels is of no value in the detection of smokers at high-risk for the development of smoking-related diseases or in the measurement of the potential protective activity of antioxidant supplementation. However, measurement of FMLP-activated LECL responses of whole blood may be useful in achieving these objectives.

L11 ANSWER 14 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 19 Mar 1988
ACCESSION NUMBER: 1988:87856 HCAPLUS Full-text
DOCUMENT NUMBER: 108:87856
ORIGINAL REFERENCE NO.: 108:14319a,14322a
TITLE: Augmentation of lung antineutrophil elastase capacity with recombinant human α-1-antitrypsin
AUTHOR(S): Casolaro, M. A.; Fells, G.; Wewers, M.; Pierce, J. E.; Ogushi, F.; Hubbard, R.; Sellers, S.; Forstrom, J.; Lyons, D.; et al.
CORPORATE SOURCE: Lab. Anim. Med. Surg., Natl. Heart, Lung, Blood Inst., Bethesda, MD, 20892, USA
SOURCE: Journal of Applied Physiology (1987), 63(5), 2015-23
CODEN: JAPHEV; ISSN: 8750-7587
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To evaluate the potential use of recombinant DNA-produced . alpha.-1-antitrypsin (α-1-AT) to augment the lung antineutrophil elastase defenses in α-1-AT deficiency, the kinetics of i.v. administered recombinant produced α-1-AT (rα-1-AT and purified normal human plasma α-1-AT (pα-1-AT) was compared in the blood and lung of rhesus monkeys. The rα-1-AT inhibited human neutrophil elastase with an association rate constant similar to that of pα-1-AT. Rhesus monkeys were infused i.v. with 120 mg/kg of rα-1-AT or pα-1-AT and the serum, urine, and lung epithelial lining fluid (ELF) concns. of these mols. quantified at various intervals. Although the initial serum levels of the rα-1-AT and pα-1-AT were both dose dependent, the pα-1-AT remained in the blood for at least 4 days, whereas the rα-1-AT disappeared rapidly, such that it was barely detectable at 24 h and strikingly, although no pα-1-AT was detectable in the urine at any time, 38% of the i.v. administered rα-1-AT was excreted within 3 h. Similar to its behavior in humans, the pα-1-AT diffused into the lung such that its concentration in the ELF of the lower respiratory tract 1-4 days after infusion was .apprx.10% that in serum. Interestingly, the rα-1-AT mol. also diffused into the lung, with ELF levels at 24 h similar to that of the pα-1-AT. Furthermore, although the rα-1-AT ELF levels declined by 48 and 96 h to below those of the pα-1-AT ELF levels, the rα-1-AT ELF levels exceeded those in blood at the same time points and, like the pα-1-AT, resulted in a significant augmentation of the antineutrophil elastase capacity of the ELF. Thus, in primates, human-based rα-1-AT has very different pharmacokinetics than does human pα-1-AT, likely because of its modified charge and/or conformation. Despite this, however, the rα-1-AT does diffuse into the lung and augments the antineutrophil elastase capacity of the ELF of the lower respiratory tract, suggesting that it has potential as a therapeutic agent in the treatment of disorders such as α-1-AT deficiency.

L11 ANSWER 15 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 05 Mar 1988
ACCESSION NUMBER: 1988:68231 HCAPLUS Full-text
DOCUMENT NUMBER: 108:68231
ORIGINAL REFERENCE NO.: 108:11135a,11138a
TITLE: Pulmonary penetration of alpha1-proteinase inhibitor administered parenterally to dogs
AUTHOR(S): Smith, Robert M.; Spragg, Roger G.; Moser, Kenneth M.; Cochrane, Charles G.; Mccarren, John P.
CORPORATE SOURCE: Dep. Med., Univ. California, San Diego, CA, 92103, USA
SOURCE: American Review of Respiratory Disease (1987), 136(6), 1391-6
CODEN: ARDSBL; ISSN: 0003-0805
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To study the penetration of α,-proteinase inhibitor (A1PI) into the lungs of healthy dogs, 83 mg of active A1PI/kg was administered i.v. over 30 min followed by a bolus of 131I-A1PI. After a distribution phase, infused A1PI left the bloodstream with a half-life of 103 h. Anal. of plasma antiprotease activity demonstrated preservation of function of the infused A1PI. Lavage fluid A1PI concentration and activity were increased 24 h after infusion. Gamma camera scans demonstrated that lung, liver, and spleen acquired 131I-A1PI similarly. Excretion of desmosine did not decrease from a baseline of 157 nmol/24 h after A1PI infusion, indicating no effect of A1PI infusion on background elastolysis. I.v. administration of A1PI can raise

lung antiproteinase levels within 24 h despite the absence of preferential uptake by the lung of the infused protein.

L11 ANSWER 16 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 27 Oct 1984
ACCESSION NUMBER: 1984:545593 HCAPLUS Full-text
DOCUMENT NUMBER: 101:145593
ORIGINAL REFERENCE NO.: 101:21969a,21972a
TITLE: Emphysema induced by intravenously administered endotoxin in an alpha1-antitrypsin-deficient rat model
AUTHOR(S): Blackwood, R. A.; Moret, J.; Mandl, I.; Turino, G. M.
CORPORATE SOURCE: Coll. Physicians and Surgeons, Columbia Univ., New York, NY, USA
SOURCE: American Review of Respiratory Disease (1984), 130(2), 231-6
CODEN: ARDSBL; ISSN: 0003-0805
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effect of repeated i.v. injections of Escherichia coli endotoxin on lung structure and parenchyma elastin proportions was studied in rats rendered deficient in .alpha.1-antitrypsin [9041-92-3] by administration of galactosamine. Within 24 h after endotoxin administration, polymorphonuclear leukocyte sequestration was demonstrable by microscopy and differential cell counts of pulmonary lavage fluid. Measurement of the proportions of elastin in lung parenchyma at 24 h revealed values in the normal range; 10 wk after repeated galactosamine and endotoxin administration, there was a reduction in the proportions of lung parenchymal elastin. At 10 wk, these animals showed a significant increase in the mean linear intercept and pulmonary compliance. Animals treated with endotoxin alone developed some but not all of the changes seen in the animals deficient in α1-antitrypsin.

L11 ANSWER 17 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1981:418818 HCAPLUS Full-text
DOCUMENT NUMBER: 95:18818
ORIGINAL REFERENCE NO.: 95:3221a,3224a
TITLE: Influence of oral contraceptives of differing dosages on α-1-antitrypsin, γ-glutamyltransferase and alkaline phosphatase
AUTHOR(S): Herbeth, B.; Bagrel, A.; Dalo, B.; Siest, G.; Leclerc, J.; Rauber, G.
CORPORATE SOURCE: Cent. Med. Prev., Vandoeuvre-les-Nancy, 54500, Fr.
SOURCE: Clinica Chimica Acta (1981), 112(3), 293-9
CODEN: CCATAR; ISSN: 0009-8981
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of oral contraceptives on blood levels of 3 glycoproteins, α-1-antitrypsin (A1AT) [9041-92-3] γ-glutamyltransferase (GGT) [9046-27-9] and alkaline phosphatase (AP) [9001-78-9] were studied in terms of age (20-40 yr), duration of administration, and levels of estrogens. Oral contraceptives increased the concentration of A1AT and the activity of GGT and decreased the

activity of AP but the changes were less pronounced for GGT and AP with pills containing low levels of estrogens. A decrease in A1AT and GGT was obsd .after 2 and 5 yr of treatment, resp., but an increase occurred in AP. Patient age seemed to have little influence on the change in AP activity and A1AT concentration but GGT activity was higher for the 25-30 yr group.

L11 ANSWER 18 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1980:511131 HCAPLUS Full-text
DOCUMENT NUMBER: 93:111131
ORIGINAL REFERENCE NO.: 93:17765a,17768a
TITLE: Inhibitory effects of α1-antitrypsin derived asialooligosaccharides on the liver uptake of the asialoglycoprotein
AUTHOR(S): Gan, Jose C.
CORPORATE SOURCE: Dep. Human Biol. Chem. Genet., Univ. Texas Med. Branch, Galveston, TX, 77550, USA
SOURCE: International Journal of Biochemistry (1980), 11(6), 481-6
CODEN: IJBOBV; ISSN: 0020-711X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB After i.v. injection into rats of . alpha.1-antitrypsin-derived oligosaccharides, asialooligosaccharides and asialoglycopeptides, but not the undesialylated materials, were rapidly taken up by the liver. Injection of labeled asialo-α1-antitrypsin with either asialooligosaccharides or asialoglycopeptides competitively inhibited liver uptake, whereas fully sialylated derivs. did not inhibit uptake. Periodate oxidation expts. with the asialooligosaccharide showed that integrity of the exposed galactose residue was required for recognition and uptake by the liver.

L11 ANSWER 19 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1980:178601 HCAPLUS Full-text
DOCUMENT NUMBER: 92:178601
ORIGINAL REFERENCE NO.: 92:28919a,28922a
TITLE: Development of an animal model of functional alpha1-antiprotease deficiency
AUTHOR(S): Eliraz, A.; Abrams, W. R.; Meranze, D. R.; Kimbel, P.; Weinbaum, G.
CORPORATE SOURCE: Med. Cent., Pulmonary, MIH, Philadelphia, PA, USA
SOURCE: Chest (1980), 77(2, Suppl.), 278
CODEN: CHETBF; ISSN: 0012-3692
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A dog model of functional .alpha.1- antiproteinase deficiency was developed by using i. v. administration of chloramine T.

L11 ANSWER 20 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1980:92202 HCAPLUS Full-text
DOCUMENT NUMBER: 92:92202
ORIGINAL REFERENCE NO.: 92:15067a,15070a
TITLE: α1-Antitrypsin deficiency and increased susceptibility to elastase-induced experimental emphysema in a rat model

AUTHOR(S): Blackwood, R. Alexander; Cerreta, Joseph M.; Mandl, Ines; Turino, Gerard M.
CORPORATE SOURCE: Coll. Physicians Surg., Columbia Univ., New York, NY, 10032, USA
SOURCE: American Review of Respiratory Disease (1979), 120(6), 1375-9
CODEN: ARDSBL; ISSN: 0003-0805
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The administration of 200 mg of D-galactosamine/kg i.p. to rats decreased the serum concns. of trypsin- and elastase-inhibiting activities. Induction of emphysema by i.v. injection of pancreatic elastase increased the severity of the disease in the animals depleted of .alpha.1- antitrypsin. The severity of the disease was correlated with trypsin- and elastase-inhibiting capacities at the time of elastase injection.

L11 ANSWER 21 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1979:70408 HCAPLUS Full-text
DOCUMENT NUMBER: 90:70408
ORIGINAL REFERENCE NO.: 90:11143a,11146a
TITLE: α1-Antitrypsin is an effector of immunological stasis
AUTHOR(S): Arora, Prince K.; Miller, Harold C.; Aronson, Lawrence D.
CORPORATE SOURCE: Dep. Microbiol. Public Health, Michigan State Univ., East Lansing, MI, USA
SOURCE: Nature (London, United Kingdom) (1978), 274(5671), 589-90
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: English

AB .alpha.1-Antitrypsin (I) (250-1000 μg, i.v.) plus 107 sheep red blood cells administered to BCF1 mice suppressed the plaque response dose-dependently, and 100-1000 μg I reduced the plaque response when its effects were studied in vitro using spleen cell cultures. Kinetic studies indicated that exposure to I for 48 h produced a reduction in plaque number, a further decrease being observed when exposure was continued for <5 days. The immunoregulation by I was not due to an effect on the adherent or T-cells; but I did regulate antigen-dependent B-cell responses.

L11 ANSWER 22 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1979:52871 HCAPLUS Full-text
DOCUMENT NUMBER: 90:52871
ORIGINAL REFERENCE NO.: 90:8457a,8460a
TITLE: Distribution of α1-antitrypsin in normal, granuloma, and tumor tissues in rats
AUTHOR(S): Ishibashi, Hiromi; Shibata, Katsunori; Okubo, Hideo; Tsuda-Kawamura, Kazunori; Yanase, Toshiyuki
CORPORATE SOURCE: Fac. Med., Kyushu Univ., Fukuoka, Japan
SOURCE: Journal of Laboratory and Clinical Medicine (1978), 91(4), 576-83
CODEN: JLCMAK; ISSN: 0022-2143
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purified rat α1-antitrypsin and albumin were radiolabeled and their distribution and catabolism in various tissues were studied in rats with inflammatory granuloma or transplanted sarcoma. I .v. administered labeled α 1-antitrypsin accumulated remarkably in extravascular spaces of the granuloma or sarcoma tissues. Among the normal organs examined, the lung preferentially incorporated α1-antitrypsin. Furthermore, most of the α1-antitrypsin accumulated in these tissues remained in a trichloroacetic acid (TCA) precipitable form throughout the observation period. Since α1-antitrypsin is incorporated in large amts. into inflammatory or tumor tissues, it could play a role in regulation of inflammatory processes or in controlling the proliferation of a tumor. The studies on TCA fractionation also suggest that liver and kidney provide the main sites for degradation of this protein. Although the accumulation of labeled albumin in granuloma and sarcoma was less marked, it showed essentially the same distribution and degradation pattern as α1-antitrypsin in both morbid states.

L11 ANSWER 23 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1979:52100 HCAPLUS Full-text
DOCUMENT NUMBER: 90:52100
ORIGINAL REFERENCE NO.: 90:8309a,8312a
TITLE: Metabolism of intact and desialylated α1-antitrypsin
AUTHOR(S): Jones, E. A.; Vergalla, J.; Steer, C. J.; Bradley-Moore, P. R.; Vierling, J. M.
CORPORATE SOURCE: Natl. Inst. Arthritis Metab. Dig. Dis., Natl. Inst. Health, Bethesda, MD, USA
SOURCE: Clinical Science and Molecular Medicine (1978), 55(2), 139-48
CODEN: CSMMCA; ISSN: 0301-0538
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Radioiodinated .alpha.1-antitrypsin (I) of protease inhibitor type MM (<1 mg, i.v.) was administered to humans, and the intravascular mass was 116 mg/kg, the extravascular/intravascular pool ratio was 1.07, the fractional catabolic rate was 33.3% of the intravascular pool/day, the half-life was 4.6 days, and formation rate was 33.8 mg/day/kg. The serum concentration of I varied independently of its fractional catabolic rate, and I appeared to be catabolized in, or in close relation to, the intravascular compartment. The fractional plasma disappearance rate of 131I-labeled, desialylated I was .apprx.150 times as great as that for the intact protein, and coincided with a rapid uptake of radioactivity by the liver. Receptor sites for desialylated glycoproteins are probably present in the surface membranes of human hepatocytes. The catabolism of I can be influenced by the structure of its carbohydrate moiety.

L11 ANSWER 24 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1978:118361 HCAPLUS Full-text
DOCUMENT NUMBER: 88:118361
ORIGINAL REFERENCE NO.: 88:18565a,18568a
TITLE: Biologic half-life and organ distribution of radiolabeled human PiM and PiZ alpha-1-antitrypsin in the dog
AUTHOR(S): Moser, Kenneth M.; Kidikoro, Yasuko; Marsh, James; Sgroi, Vincent
CORPORATE SOURCE: Dep. Med., Univ. California Sch. Med., La Jolla,

CA, USA
SOURCE: Journal of Laboratory and Clinical Medicine (1978), 91(2), 214-22
CODEN: JLCMAK; ISSN: 0022-2143
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Highly purified .alpha.1-antitrypsin from blood of donors of known PiZZ and PiMM phenotype was radiolabeled with 125I or 131I and injected i.v. into dogs. The radiolabeled proteins retained their prelabel electrophoretic and trypsin-inhibitory characteristics. The biologic half-life of both M and Z protein in the circulation were similar, averaging 71 h for M protein and 80 h for Z protein. The label remained tightly bound in vivo for 2 days after injection. The material was nonpyrogenic in rabbit and dog. No arteriovenous differences in radioactivity could be detected at 2 or 20 min after injection. However, surface scanning disclosed substantial pulmonary deposition of radioactivity for the first 9 h after injection. At 48 h, intense radioactivity was present in the spleen, but not in the liver. Thus similar studies appear feasible in man, including noninvasive assessment of body distribution of M and Z protein by surface scanning techniques.

L11 ANSWER 25 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1977:420123 HCAPLUS Full-text
DOCUMENT NUMBER: 87:20123
ORIGINAL REFERENCE NO.: 87:3185a,3188a
TITLE: Serum trypsin inhibitors and autoantibody titer to it in hypertrypsinemia
AUTHOR(S): Protsenko, V. A.; Dotsenko, S. M.; Karpitskii, V. V.; Spitsin, I. F.
CORPORATE SOURCE: Krym. Med. Inst., Simferopol, USSR
SOURCE: Patologicheskaya Fiziologiya i Eksperimental'naya Terapiya (1976), (2), 77-8
CODEN: PAFEAY; ISSN: 0031-2991
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB In dogs and rabbits after i.v. injection of crystalline trypsin (0.5 mg/kg body weight) the serum activity of proteinases increased 30 and 60 min and antitrypsin activity and trypsin auto-antibody level decreased 30 min and normalized 60 min after the injection.

L11 ANSWER 26 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1977:118231 HCAPLUS Full-text
DOCUMENT NUMBER: 86:118231
ORIGINAL REFERENCE NO.: 86:18665a,18668a
TITLE: The role of sialic acid and galactose residues in determining the survival of human plasma α1-antitrypsin in the blood circulation
AUTHOR(S): Yu, Shi-Da; Gan, Jose C.
CORPORATE SOURCE: Med. Branch, Univ. Texas, Galveston, TX, USA
SOURCE: Archives of Biochemistry and Biophysics (1977), 179(2), 477-85
CODEN: ABBIA4; ISSN: 0003-9861
DOCUMENT TYPE: Journal
LANGUAGE: English
AB After an i.v. injection of intact (NANA-7)-α1-AT (periodate-oxidized, tritiated, borohydride-reduced .alpha.1-antitrypsin) into rats, the labeled material had a circulating half-life of

18 h. When (NANA-7)-α1-AT was partially desialylated (4 residues of NANA-7 out of a total of 6 were removed, thus exposing an equivalent number of galactose residues at the terminal positions) by neuraminidase, injection into rats of this material resulted in a rapid and almost complete disappearance of the label from the circulation in 60 min. There was a concomitant accumulation of radioactivity in the liver. The rate of this rapid transfer depended on the presence of intact galactose residues as the terminal, nonreducing sugar in the carbohydrate units. Galactose oxidase treatment of the partially desialylated (NANA-7)-α1-AT, which presumably oxidized the primary alc. of galactose at C-6 to an aldehyde group, caused a reversion of its survival time in the circulation to that of the intact (NANA-7)-α1-AT.

L11 ANSWER 27 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1976:540475 HCAPLUS Full-text
DOCUMENT NUMBER: 85:140475
ORIGINAL REFERENCE NO.: 85:22523a,22526a
TITLE: The disappearance of enzyme-inhibitor complexes from the circulation of man
AUTHOR(S): Ohlsson, K.; Laurell, C. B.
CORPORATE SOURCE: Univ. Lund, Malmoe Gen. Hosp., Malmoe, Swed.
SOURCE: Clinical Science and Molecular Medicine (1976), 51(1), 87-92
CODEN: CSMMCA; ISSN: 0301-0538
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Following i.v. administration of complexes of human trypsin and human granulocyte elastase with . alpha.1-anti-trypsin and α2-macroglobulin into human volunteers, elimination of α2-macroglobulin complexes with trypsin and elastase followed single-exponential functions with half-lives of 9 and 12 min resp. Complexes of α1-anti-trypsin with trypsin and elastase had half-lives of 3.5 and 1 hr resp. The α1-anti-trypsin complexes dissociated and the trypsin and elastase transferred to α2-macroglobulin. α2-Macroglobulin may have a protective action against endogenous proteases.

L11 ANSWER 28 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1975:557664 HCAPLUS Full-text
DOCUMENT NUMBER: 83:157664
ORIGINAL REFERENCE NO.: 83:24671a
TITLE: Intestinal absorption and biotransformation of elastase
AUTHOR(S): Katayama, Kouichi; Fujita, Takeshi
CORPORATE SOURCE: Res. Dev. Div., Eisai Co., Ltd., Tokyo, Japan
SOURCE: Proc. Symp. Drug Metab. Action, 5th (1974***) , Meeting Date 1973, 87-104. Editor(s): Murata, Toshiro. Pharm. Soc. Jpn.: Tokyo, Japan.
CODEN: 30GLA6
DOCUMENT TYPE: Conference
LANGUAGE: English
AB After intraintestinal administration to rats, 0.150 and 0.053%, resp., of 1 and 5 mg doses of 131I-labeled elastase (EC 3.4.4.7) [9004-06-2] was absorbed via the portal vein and lymphatics. Absorption of elastase via lymphatics was 36% of the total absorbed. Elastase bound to the blood serum proteins, α2-macroglobulin (α2M) and . ***alpha.1-antitrypsin (.alpha

.1ATr) [9041-92-3] both in vitro and after i.v. injecton at 0.3 mg/kg. Elastase bound to α2M was cleared from the blood approx. 20 times faster than elastase bound to α1ATr. In addn., the elastase bound to α2M was taken up in the liver, more specifically, the 27,000 xg fraction; elastase bound to α1ATr was distributed widely to all of the tissues tested and was slowly taken up in the liver. In the 27,000 xg fraction of liver (heterolysosomes), injected elastase was degraded to 131I-labeled iodotyrosine [60-18-4] by the lysosomal proteinases, cathepsin D [9025-26-7] and cathepsin B1 [9047-22-7]. However, the radioactivity excreted in urine mainly consisted of inorg. 131I.

L11 ANSWER 29 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1975:510797 HCAPLUS Full-text
DOCUMENT NUMBER: 83:110797
ORIGINAL REFERENCE NO.: 83:17393a,17396a
TITLE: Protein turnover studies using in vivo labeling and immunoprecipitation
AUTHOR(S): Johnson, A. M.; McMillan, C. W.
CORPORATE SOURCE: Sch. Med., Univ. North Carolina, Chapel Hill, NC, USA
SOURCE: Clinica Chimica Acta (1975), 62(2), 363-9
CODEN: CCATAR; ISSN: 0009-8981
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The feasibility of immunochem. precipitation of radiolabeled proteins from plasma or serum samples was evaluated by using selenomethionine-75Se injected i.v. into humans and rabbits and by the determination of the radioactivity of antiserum-precipitated fibrinogen, haptoglobin, .alpha.1-antitrypsin, and immunoglobulin G (IgG). Good correlations were obtained between parallel fibrinogen studies using a standard clotting technique and immunopptn. Single studies of haptoglobin, α1-antitrypsin, and IgG suggested that nonspecific precipitation was not a major problem in this method since the plasma half-times were quite divergent and compared favorably with those obtained by using in vitro labeling with 125I or 131I. The method was useful apparently for studying the turnover of plasma proteins that are difficult to study because of problems in purification or in vitro labeling.

L11 ANSWER 30 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1975:153121 HCAPLUS Full-text
DOCUMENT NUMBER: 82:153121
ORIGINAL REFERENCE NO.: 82:24443a,24446a
TITLE: Clinical significance of α1-antitrypsin
AUTHOR(S): Stocker, W.; Sasse, I.; Rentsch. I.
CORPORATE SOURCE: III. Med. Klin. Mannheim, Mannheim, Fed. Rep. Ger.
SOURCE: Therapiewoche (1974), 24(52), 6142, 6145
CODEN: THEWA6; ISSN: 0040-5973
DOCUMENT TYPE: Journal; General Review
LANGUAGE: German

AB A review, with no refs. The serum level of α- antitrypsin (I) is elevated in all inflammatory diseases, in the postoperative state, in pregnancy, and during the administration of oral contraceptives; also in neoplasias with extended tissue obstruction, aseptic necroses (myocardial infarction, and cryoglobulinemia). No alterations were observed in allergies and leukoses.

The assay of I for differential diagnostic purposes is therefore not relevant. A decrease of I was observed in the terminal state of severe renal diseases with elevated protein loss and in hepatic diseases with a disturbed protein synthesis. In about 5% of healthy humans a genetic decrease of I was found. The importance of the serum content of I in homozygotic and heterozygotic dysproteinemic defects with respect to bronchopulmonary diseases is also discussed.

L11 ANSWER 31 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1974:445953 HCAPLUS Full-text
DOCUMENT NUMBER: 81:45953
ORIGINAL REFERENCE NO.: 81:7325a,7328a
TITLE: Biotransformation of elastase. III. Effects of elastase-binding proteins in serum on the disappearance of iodine-131-labeled elastase from blood
AUTHOR(S): Katayama, Kouichi; Fujita, Takeshi
CORPORATE SOURCE: Res. Dev. Div., Eisai Co., Ltd., Tokyo, Japan
SOURCE: Biochimica et Biophysica Acta, Protein Structure (1974), 336(2), 165-77
CODEN: BBPTBH; ISSN: 0005-2795
DOCUMENT TYPE: Journal
LANGUAGE: English
AB I.v. injection of elastase (EC 3.4.4.7) [9004-06-2] into rats resulted in the enzyme binding with the serum proteins, α2-macroglobulin and .alpha.1-antitrypsin. The degree of dissociation of the α2-macroglobulin-elastase and α1-antitrypsin-elastase complexes in rat serum after incubation for 6 hr at 37.deg. was 8.9 and 15.4%, resp. The half-life in the transfer of α2-macroglobulin-elastase and α1-antitrypsin-elastase complexes to the site of degradation was 9.38 min and 3.06 hr, resp.

L11 ANSWER 32 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1972:10744 HCAPLUS Full-text
DOCUMENT NUMBER: 76:10744
ORIGINAL REFERENCE NO.: 76:1749a,1752a
TITLE: In vivo interaction between α-chymotrypsin and plasma proteins in the dog
AUTHOR(S): Ohlsson, K.
CORPORATE SOURCE: Dep. Clin. Chem., Malmo Gen. Hosp., Malmo, Swed.
SOURCE: Scandinavian Journal of Clinical and Laboratory Investigation (1971), 28(1), 13-19
CODEN: SJCLAY; ISSN: 0036-5513
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Small amts. of bovine, 125I-labeled α-chymotrypsin injected i.v. into dogs were bound to . alpha.1-antitrypsin (about 85%) and the remainder to α-macroglobulin. The injection of larger amts. decreased the concentration of α-macroglobulin. Chymotrypsin-α-macroglobulin complexes were rapidly eliminated from the blood. There was a transfer of chymotrypsin from the complex to both α-macroglobulins. Dogs did not show any signs of a general reaction before the α1-antitrypsin had been saturated with chymotrypsin. Thereafter, there was a tendency to shock and hypercoagulability followed by fibrinolysis and death. It is concluded that α1-antitrypsin is a stronger inhibitor of chymotrypsin than of trypsin.

L11 ANSWER 33 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1972:2449 HCAPLUS Full-text
DOCUMENT NUMBER: 76:2449
ORIGINAL REFERENCE NO.: 76:457a,460a
TITLE: Interactions in vitro and in vivo between dog trypsin and dog plasma protease inhibitors
AUTHOR(S): Ohlsson, K.
CORPORATE SOURCE: Dep. Clin. Chem., Malmo Gen. Hosp., Malmo, Swed.
SOURCE: Scandinavian Journal of Clinical and Laboratory Investigation (1971), 28(2), 219-23
CODEN: SJCLAY; ISSN: 0036-5513
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Trace amts. of dog trypsin (I) mixed with dog serum or injected i.v. into the dog were bound mainly to the α-macroglobulins (82) and to α 1-antitrypsin (18). The relative affinity of I for the α-macroglobulins was about 30 times as high as for the other inhibitors taken together. I bound to α1-antitrypsin was rapidly taken over by the α-macroglobulins in vitro as well as in vivo. The I-α-macroglobulin complexes injected i.v. or formed in vivo were rapidly eliminated from the blood stream, following a 1st order reaction, while .alpha .1-antitrypsin-bound I disappeared much slower as found for bovine trypsin and dog plasma trypsin inhibitors.

L11 ANSWER 34 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 22 Apr 2001
ACCESSION NUMBER: 1963:16793 HCAPLUS Full-text
DOCUMENT NUMBER: 58:16793
ORIGINAL REFERENCE NO.: 58:2766d-e
TITLE: The mechanism of antiedematous action of parenterally administered crystalline proteinases
AUTHOR(S): Veremeenko, K. N.
CORPORATE SOURCE: Inst. Biochem., Acad. Sci. Ukr. S.S.R., Kiev
SOURCE: Voprosy Meditsinskoi Khimii (1962), 8, 525-31
CODEN: VMDKAM; ISSN: 0042-8809
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Parenterally administered crystalline prepns. of trypsin (I) and chymotrypsin (II) inhibit the development of exptl. edema caused by egg albumin injections in rats. Combined treatment with both I and II, in doses which were ineffective sep., inhibits edema formation. Acetylated I was a slightly less active antiedematous agent than I. The existence of a correlation between proteolytic activity of I and II and their antiedematous effect was shown. I administered to rabbits in a dose of 5-15 mg./kg. intramuscularly did not influence the antitrypsin activity of blood serum during the 1st day. In 2 days the antitrypsin activity slightly increased.

L11 ANSWER 35 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 22 Apr 2001
ACCESSION NUMBER: 1961:9454 HCAPLUS Full-text
DOCUMENT NUMBER: 55:9454
ORIGINAL REFERENCE NO.: 55:1895g
TITLE: Acute pancreatitis and enzymic toxemia. Antitrypsin

AUTHOR(S): Bernard, Adolphe
SOURCE: Presse Medicale (1893-1971) (1959), 67, 2351-3
CODEN: PRMEAI; ISSN: 0032-7867
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Two dogs underwent pancreatic trypsin infusion. One of them received intravenous injections of antitrypsin and an antihistaminic; glycemia and amylasemia remained unchanged. In the other dog these values increased.

L11 ANSWER 36 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 22 Apr 2001
ACCESSION NUMBER: 1958:62309 HCAPLUS Full-text
DOCUMENT NUMBER: 52:62309
ORIGINAL REFERENCE NO.: 52:11262c-e
TITLE: Changes in serum antitrypsin in rabbits after intravenous trypsin administration
AUTHOR(S): Polcak, J.; Sevelova, D.; Votava, L.; Sevela, M.
CORPORATE SOURCE: Masaryk Univ., Brno, Czech.
SOURCE: Scripta Med. Fac. Med. Univ. Brunensis et Palackyanae (1957), 30, 283-90
DOCUMENT TYPE: Journal
LANGUAGE: Czech/English
AB The decrease in the amount of antitrypsin (I) was roughly proportional to the amount of injected trypsin (II) (doses 3-12.7 mg./kg. body weight). When heparin (III) (1000-5000 units) was administered before II (10-46.2 mg./kg.) the level of I decreased, but in half the cases the decrease was less than expected. No inhibition of II by III was observed in vitro.

L11 ANSWER 37 OF 37 HCAPLUS COPYRIGHT 2009 ACS on STN
ED Entered STN: 16 Dec 2001
ACCESSION NUMBER: 1937:62090 HCAPLUS Full-text
DOCUMENT NUMBER: 31:62090
ORIGINAL REFERENCE NO.: 31:8569i,8570a
TITLE: Acid-base equilibrium and the serum enzymes
AUTHOR(S): Mori, Fumihiko
SOURCE: Sei-I-Kai Medical Journal (1937), 56(No. 2), 218-76(English abstr. 5-6)
CODEN: SMEJAP; ISSN: 0371-1080
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB When the acid-base balance is disturbed in rabbits by oral administration of either acid phosphate (pH 3), or alkali phosphate (pH 8), antitrypsin of the serum is increased, lipase is decreased and amylase is unaffected. If neutral phosphate buffer (pH 7.1) is given instead, antitrypsin is also increased, the other two are unaffected. Starvation for 3 days causes a change similar to that of the neutral buffer.

FILE 'MEDLINE' ENTERED AT 15:58:55 ON 18 MAY 2009

FILE 'BIOSIS' ENTERED AT 15:58:55 ON 18 MAY 2009

FILE 'EMBASE' ENTERED AT 15:58:55 ON 18 MAY 2009

FILE 'WPIX' ENTERED AT 15:58:55 ON 18 MAY 2009

COPYRIGHT (C) 2009 THOMSON REUTERS

FILE 'JAPIO' ENTERED AT 15:58:55 ON 18 MAY 2009
COPYRIGHT (C) 2009 Japanese Patent Office (JPO)- JAPIO

FILE 'PASCAL' ENTERED AT 15:58:55 ON 18 MAY 2009
Any reproduction or dissemination in part or in full,
by means of any process and on any support whatsoever
is prohibited without the prior written agreement of INIST-CNRS.
COPYRIGHT (C) 2009 INIST-CNRS. All rights reserved.

FILE 'DISSABS' ENTERED AT 15:58:55 ON 18 MAY 2009
COPYRIGHT (C) 2009 ProQuest Information and Learning Company; All Rights Res
erved.

FILE 'LIFESCI' ENTERED AT 15:58:55 ON 18 MAY 2009
COPYRIGHT (C) 2009 Cambridge Scientific Abstracts (CSA)

FILE 'BIOTECHDS' ENTERED AT 15:58:55 ON 18 MAY 2009
COPYRIGHT (C) 2009 THOMSON REUTERS

FILE 'SCISEARCH' ENTERED AT 15:58:55 ON 18 MAY 2009
Copyright (c) 2009 The Thomson Corporation

FILE 'BIOTECHABS' ACCESS NOT AUTHORIZED

FILE 'BIOTECHNO' ENTERED AT 15:58:55 ON 18 MAY 2009
COPYRIGHT (C) 2009 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'PROMT' ENTERED AT 15:58:55 ON 18 MAY 2009
COPYRIGHT (C) 2009 Gale Group. All rights reserved.

FILE 'RDISCLOSURE' ENTERED AT 15:58:55 ON 18 MAY 2009
COPYRIGHT (C) 2009 Kenneth Mason Publications Ltd.

L12 29 SEA ABB=ON PLU=ON L2(10A)((ADMIN? OR INJECT? OR APPLICATI ON OR APPLY? OR APPLIED)(10A)(OSMOTIC?(W) PUMP OR INHALE# OR INHALANT OR INHALING OR INHALATION?))
L13 42 SEA ABB=ON PLU=ON L2(10A)((ADMIN? OR INJECT? OR APPLICATI ON OR APPLY? OR APPLIED)(10A)(INTRAMUSCUL? OR SUBCUTANEOUS? OR INTRATHECAL? OR EPIDURAL? OR TRANSDERMAL? OR INTRACEREB ROVENTRIC?))
L14 189 SEA ABB=ON PLU=ON L2(10A)((ADMIN? OR INJECT? OR APPLICATI ON OR APPLY? OR APPLIED)(10A)(PARENTAL? OR ORAL? OR MOUTH OR VAGINAL? OR RECTAL? OR ANAL OR NASAL? OR MOSE OR BUCCAL? OR INTRAVENOUS? OR IV OR I V OR INTRA(W)(VENOUS? OR MUSCUL? OR CEREBROVENTRIC?)))
L15 243 SEA ABB=ON PLU=ON ((L12 OR L13 OR L14)) NOT L9
L16 117 SEA ABB=ON PLU=ON L15 AND (PY<2000 OR AY<2000 OR PRY<2000)
L17 63 SEA ABB=ON PLU=ON L16 AND (TREAT? OR THERAP? OR PREVENT?)
L18 29 DUP REM L17 (34 DUPLICATES REMOVED)

L18 ANSWER 1 OF 29 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 1
ACCESSION NUMBER: 1999:460730 BIOSIS Full-text
DOCUMENT NUMBER: PREV199900460730
TITLE: Emphysema: New concepts.
AUTHOR(S): Mal, Herve [Reprint author]; Crestani, Bruno; Aubier,

Michel; Fournier, Michel
CORPORATE SOURCE: Service de pneumologie et reanimation respiratoire, Hopital Beaujon, 100, avenue du General-Leclerc, 92118, Clichy Cedex, France
SOURCE: M-S (Medecine Sciences), (June-July, 1999) Vol. 15, No. 6-7, pp. 833-841. print.
ISSN: 0767-0974.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: French
ENTRY DATE: Entered STN: 1 Nov 1999
Last Updated on STN: 1 Nov 1999

AB Pathophysiologic and therapeutic concepts concerning lung emphysema are evolving. The old pathophysiologic concept is based upon the hypothesis that emphysema is the consequence of an imbalance between the proteases released by neutrophils and the anti-proteases shield in the alveolar space that allows the destruction of elastin fibers. Recent data suggest (1) that proteases secreted by alveolar macrophages might be more relevant to the pathogenesis of the disease than that released by neutrophils (2) that collagenolytic enzymes might participate to the destruction process within the lung as well as elastolytic protease, (3) that the repair of elastin and collagen fibersoccurs in the lung simultaneously to their destruction, at least in animal models of emphysema, and (4) that repair is possible in a rat model of elastase-induced emphysema using all trans-retinoic acid. Therapeutic options in human emphysema are also evolving. Increasing the antiprotease alveolar shield through the intravenous or inhaled administration of alpha-1-antitrypsin in selected patients with genetical alpha-1-antitrypsin deficiency is used worldwide in selected patients despite the lack of scientific evidence of efficacy. Surgical treatments have been developed in the past 10 years and are currently under investigation. Lung transplantation is used in patients with severe airway obstruction on lung function tests and functionally disabled. Its beneficial effect in terms of survival is not prove but quality of life is improved with the technique. Lung volume reduction surgery improves dyspnea, lung function and gas exchange in most patients, but long term beneficial effects, selection criteria of the patients are currently unknown.

L18 ANSWER 2 OF 29 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2000238489 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 10776189
TITLE: Alpha 1-antitrypsin deficiency and the impact of nursing interventions and treatment with intravenous therapy. An overview.
AUTHOR: Scharnweber K
CORPORATE SOURCE: Healthsouth Rehabilitation Hospital, Arlington, Texas, USA.
SOURCE: Journal of intravenous nursing : the official publication of the Intravenous Nurses Society, (1999 Sep-Oct) Vol. 22, No. 5, pp. 258-64.
Ref: 34
Journal code: 8804311. ISSN: 0896-5846.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Nursing Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 6 Jul 2000
Last Updated on STN: 6 Jul 2000

Entered Medline: 29 Jun 2000

AB The primary function of alpha1-antitrypsin is to protect the alveoli in the lung from harmful destruction from proteolytic enzymes, which prevent optimal elastic recoil of the lungs and destroy the lungs. Insufficient serum levels of alpha1-antitrypsin eventually lead to early onset of emphysema in the third, fourth, or fifth decade of life. Treatment of alpha1-antitrypsin deficiency by intravenous administration of an enzyme inhibitor known as alpha1-proteinase inhibitor, a human-derived blood product, can be administered to help replace the enzymes required to maintain lung function. Early detection, nursing intervention, and clinical management slow the progression of this hereditary disease.

L18 ANSWER 3 OF 29 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 1999:280652 BIOSIS Full-text
DOCUMENT NUMBER: PREV199900280652
TITLE: Alpha-1-protease inhibitor deficiency and pulmonary emphysema as viewed by pulmonary specialists in private praxis.
AUTHOR(S): Wencker, Marion [Reprint author]; Konietzko, N.
CORPORATE SOURCE: Kuhlmannsfeld 53, D-45355, Essen, Germany
SOURCE: Atemwegs- und Lungenkrankheiten, (Feb., 1999) Vol. 25, No. 2, pp. 89-95. print.
CODEN: ATLUDF. ISSN: 0341-3055.
DOCUMENT TYPE: Article
LANGUAGE: German
ENTRY DATE: Entered STN: 28 Jul 1999
Last Updated on STN: 28 Jul 1999

AB In a multicenter mail survey 210 pneumologists or internal medicine physicians specialized on pneumology in private praxis were asked about their experience with pulmonary emphysema, particularly referring to alpha-1-protease inhibitor (alpha1-Pi) deficiency. The mean percentage of patients with pulmonary emphysema seen by pulmonary specialists in private praxis was 17%, a total of 5% of the patients had clinically relevant emphysema. The main reason for referral to the pulmonary specialist was the worsening of the patient despite therapy. Additionally to a physical examination, pulmonary function tests, blood gas analysis, and chest X-ray, 67% of the physicians included the determination of serum alpha1-Pi levels as a routine diagnostic method in suspected pulmonary emphysema. Approximately 2.7% or 3 patients with emphysema suffered from severe alpha1-Pi deficiency. 51% of the respiratory specialists had experience with intravenous augmentation therapy with human alpha1-Pi (Prolastin HS) andthe vast majority applied 60 mg/kg body weight once weekly. 56% of the pulmonary specialists reported a stabilization of pulmonary function due to augmentation therapy and 31% thought it was too early to evaluate the effect. The therapeutic intervention in patients with severe alpha1-Pi deficiency includes strict non-smoking, vaccination against influenza and pneumococci, vigorous treatment of pulmonary infections and avoiding harmful smokes and fumes.

L18 ANSWER 4 OF 29 PROMT COPYRIGHT 2009 Gale Group on STN

ACCESSION NUMBER: 97:28399 PROMT Full-text
TITLE: Inhale and Centeon Enter Into Development and Licensing Agreement for Alpha-1 Proteinase Inhibitor.
SOURCE: Business Wire, (13 Jan 1997) pp. 1131122.
LANGUAGE: English
WORD COUNT: 597
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB PALO ALTO, Calif.--(BUSINESS WIRE)--Jan. 13, 1997--Inhale Therapeutic Systems (NASDAQ:INHL) and Centeon L.L.C. today announced that they have entered into a collaboration to develop a pulmonary formulation of alpha-1 proteinase inhibitor to treat patients with alpha-1 antitrypsin deficiency, a genetic disorder which can lead to emphysema. In the agreement, Centeon will receive commercialization rights worldwide outside of Japan, and Inhale will receive royalties on product sales, an up-front signing fee and up to an estimated $15 million in R&D funding and milestone payments. Centeon will manufacture the active ingredient for use in Inhale's deep-lung delivery device for macromolecules. Inhale will manufacture and package the dry powder, and supply inhalation devices to Centeon for commercialization and marketing.

The two companies also announced that they have completed pre-clinical work that indicates Inhale's dry powder formulation of Centeon's alpha-1 proteinase inhibitor has the potential to significantly improve the efficiency of delivery compared to current infusion therapy. Alpha-1 proteinase inhibitor is approved in the United States and several other countries for treatment of alpha-1 antitrypsin deficiency, a condition believed to affect as many as 100,000 people in the US with additional numbers in Europe. The drug is currently approved for weekly intravenous infusion. A pulmonary-delivered therapy could be a significant improvement in therapeutic efficiency and delivery convenience. "Centeon's mission is to pioneer scientific innovation to supply effective, high quality therapies that improve and extend the lives of patients throughout the world. An alpha- 1 proteinase inhibitor delivered via the pulmonary route could be a major breakthrough in greatly improving patient quality of life," said John Sedor, CEO of Centeon. "We believe Inhale has the leading technology in pulmonary delivery of macromolecules such as alpha-1 proteinase inhibitor, and we are excited to be working with them on this project."

"Centeon is an excellent partner for Inhale for alpha-1 proteinase inhibitor," said Robert Chess, president and CEO of Inhale. "Centeon is the global leader in the plasma protein industry and has outstanding capabilities in research, development and marketing." THIS IS AN EXCERPT: COPYRIGHT 1997 Business Wire

L18 ANSWER 5 OF 29 BIOTECHDS COPYRIGHT 2009 THOMSON REUTERS on STN
ACCESSION NUMBER: 1997-08134 BIOTECHDS Full-text
TITLE: Adeno virus vector-infected cells can escape adeno virus antigen-specific cytotoxic T-lymphocyte killing in vivo; alpha-1-antitrypsin gene transfer to mouse as a model for gene therapy
AUTHOR: Wadsworth S C; Zhou H; Smith A E; Kaplan J M
CORPORATE SOURCE: Genzyme; Baylor-Coll.Med
LOCATION: Genzyme Corporation, 1 Mountain Road, Framingham, MA 01701, USA.
Email: swadsworth@genzyme.com
SOURCE: J.Virol.; (1997) 71, 7, 5189-96
CODEN: JOVIAM
ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English
AN 1997-08134 BIOTECHDS Full-text
AB The adeno virus (Ad)-specific cytotoxic T-lymphocyte (CTL) response to a first generation vector expressing human alpha- 1-antitrypsin (huAAT) as the reporter gene product was examined in mice. Injection (i.v.) of Ad vector encoding huAAT stimulated an Ad-specific cellular immune response but failed to abolish vector-directed gene expression in vivo, and the vector directed non-immunogenic transgene expression for long periods in C57BL/6 mice, despite the presence of circulating CTL specific for Ad antigens. When Ad levels were boosted, there was no detectable impact on the persistence of

AdhuAAt expression. Thus, expression of Ad vector antigens appears to be insufficient, in some circumstances, to target infected cells for CTL lysis. First generation Ad vectors may be effective for gene therapy applications.

L18 ANSWER 6 OF 29 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 1997459831 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9315791
TITLE: Pharmacokinetic study of alpha1-antitrypsin infusion in alpha1-antitrypsin deficiency.
AUTHOR: Barker A F; Iwata-Morgan I; Oveson L; Roussel R
CORPORATE SOURCE: Department of Medicine, Oregon Health Sciences University, Portland, USA.
SOURCE: Chest, {1997 Sep} Vol. 112, No. 3, pp. 607-13.
Journal code: 0231335. ISSN: 0012-3692.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 5 Nov 1997
Last Updated on STN: 3 Mar 2000
Entered Medline: 22 Oct 1997

AB OBJECTIVES: To ascertain how long 120 mg/kg alpha1- antitrypsin concentrate (alpha1-AT-C), administered I.V. every 2 weeks, can maintain alpha1-antitrypsin (alpha1-AT) serum levels above 70 to 80 mg/dL. Secondary objectives were to summarize the nature, severity, and relationship of a plasma-derived alpha1-AT-C infusion to any side effects. METHODS: This was an open-label uncontrolled pharmacokinetic study. Alpha1-AT-C was administered I.V. every 2 weeks for 10 infusions in 23 patients with PIZ alpha1-AT deficiency. Serum alpha1-AT levels and neutralizing elastase activity were measured preinfusion, postinfusion, and at nadir. During two infusion periods, daily serum alpha1-AT and neutralizing elastase activities were measured on the seventh to 14th days. Five patients received BAL assays for alpha1-AT and neutralizing elastase activity. Adverse events were recorded in a patient diary and by a nurse at each infusion visit. RESULTS: The 120-mg/kg dose of alpha1-AT-C could not maintain nadir serum protective levels above 70 or 80 mg/dL for the entire 14-day dosing interval in most patients. None of the patients had alpha1-AT levels above 80 mg/dL for all 14 days. The serum alpha1-AT and neutralizing elastase levels correlated suggesting functional activity. The BAL alpha1-AT and neutralizing elastase activities were low and did not correlate with serum levels. CONCLUSION: Alpha1-AT-C at 120 mg/kg administered every 2 weeks did not maintain nadir serum alpha1-AT levels above 70 to 80 mg/dL for a 14-day dosing interval. Higher doses every 2 weeks or decreased interval between infusions may be required.

L18 ANSWER 7 OF 29 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 1997192127 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9039946
TITLE: alpha 1-antitrypsin deficiency-associated panniculitis: resolution with intravenous alpha 1-antitrypsin administration and liver transplantation.
AUTHOR: O'Riordan K; Blei A; Rao M S; Abecassis M
CORPORATE SOURCE: Department of Medicine, Northwestern University Medical

School, Chicago, IL 60611, USA.
SOURCE: Transplantation, (1997 Feb 15) Vol. 63, No. 3, pp. 480-2.
Journal code: 0132144. ISSN: 0041-1337.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 21 Mar 1997
Last Updated on STN: 21 Mar 1997
Entered Medline: 11 Mar 1997

AB Panniculitis is a rare complication of alpha 1-antitrypsin (A1AT) deficiency that is characterized by acute inflammatory infiltrate and fat necrosis. Different treatment strategies are used to provide symptomatic relief. Here we describe two patients with homozygous A1AT deficiency who developed panniculitis and were successfully treated with A1AT replacement. The patient who received a liver transplant experienced complete resolution of the skin lesions. The patient who received A1AT intravenously showed complete response, but the skin lesions recurred when the levels of A1AT fell below 50 mg/100 ml. Panniculitis secondary to A1AT deficiency can be successfully treated with liver transplantation or intravenous infusion of A1AT.

L18 ANSWER 8 OF 29 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 5
ACCESSION NUMBER: 1996:508009 BIOSIS Full-text
DOCUMENT NUMBER: PREV199699230365
TITLE: Development of a complementing cell line and system for construction of adenovirus vectors with E1 and E2a deleted.
AUTHOR(S): Zhou, Heshan; O'Neil, Wanda; Morral, Nuria; Beaudet, Arthur L. [Reprint author]
CORPORATE SOURCE: Baylor Coll. Med., Dep. Mol. Hum. Genet., Room T619, Houston, TX 77030, USA
SOURCE: Journal of Virology, (1996) Vol. 70, No. 10, pp. 7030-7038.
CODEN: JOVIAM. ISSN: 0022-538X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Nov 1996
Last Updated on STN: 14 Nov 1996

AB Although adenovirus vectors offer many advantages, it would be desirable to develop vectors with improved expression and decreased toxicity. Toward this objective, an adenovirus vector system with deletion of both the E1 and E2a regions was developed. A 5.9-kb fragment of the adenovirus type 5 (Ad5) genome containing the E2a gene and its early and late promoters was transfected into 293 cells. A complementing cell line, designated 293-C2, expressed the E2a mRNA and protein and was found to complement the defect in Ad5 viruses with temperature-sensitive or deletion mutations in E2a. A deletion of 1.3 kb removing codons 40 to 471 of the 529 amino acids of E2a was introduced into plasmids for preparation of viruses and vectors. An Ad5 virus with disruption of the E1 gene and deletion of E2a grew on 293-C2 cells but not on 293 cells. Vectors with E1 and E2a deleted expressing Escherichia coli beta-galactosidase or human alpha -1-antitrypsin were prepared and expressed the reporter genes after intravenous injection into mice. This vector system retains sequences in common between the complementing cell line and the vectors, including 3.4 kb upstream and 1.1 kb downstream of the deletion. These vectors have potential advantages of increased capacity for insertion of

transgene sequences, elimination of expression of E2a, and possibly reduction in expression of other viral proteins. Although the titers of the vectors with deleted are about 10- to 30-fold below those of vectors with E2a wild-type regions, the former vectors are suitable for detailed studies with animals to evaluate the effects on host immune responses, on duration of expression, and on safety.

L18 ANSWER 9 OF 29 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 1996236793 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8800748
TITLE: Human alpha 1-antitrypsin gene transfer to in vivo mouse hepatocytes.
AUTHOR: Alino S F; Bobadilla M; Crespo J; Lejarreta M
CORPORATE SOURCE: Department of Pharmacology, Faculty of Medicine and Dentistry, University of Valencia, Spain.
SOURCE: Human gene therapy, (1996 Mar 1) Vol. 7, No. 4, pp. 531-6.
Journal code: 9008950. ISSN: 1043-0342.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 15 Oct 1996
Last Updated on STN: 15 Oct 1996
Entered Medline: 1 Oct 1996

AB The in vivo gene transfer to mouse hepatocytes of pTG 7101, a plasmid containing the full-length gene encoding human alpha 1-antitrypsin (alpha 1-AT) DNA, has been studied by iv administration of recombinant DNA (100 ng/mouse) encapsulated in large and small liposomes. Our results from immunohistochemical liver sections and cytophotometric analysis of hepatocyte chromophore absorbance indicate that human alpha 1-AT was expressed in liver parenchymal cells from mice treated (48 hr before) with DNA encapsulated in small liposomes, and this effect remained for at least 2 weeks. In contrast, the efficiency was greatly limited when large liposomes were used as a vehicle for gene transfer. Additional experiments were performed to study using an ELISA procedure the presence in mouse plasma of human alpha 1-AT from mice treated with encapsulated plasmid in small liposomes or small empty liposomes plus free DNA. According to the immunohistochemical data, the results indicate that detectable alpha 1-AT can only be observed in plasma from mice treated with encapsulated plasmid in small liposomes.

L18 ANSWER 10 OF 29 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 1995093515 EMBASE Full-text
TITLE: Venous thrombosis associated with protein-losing enteropathy.
AUTHOR: Sakai, R. (correspondence); Okuda, C.; Ishizuka, N.; Iwade, K.; Hosoda, S.; Hashimoto, A.; Saitou, H.; Mori, N.
CORPORATE SOURCE: Department of Cardiology, Heart Institute of Japan, Tokyo Women's Medical Hospital, Tokyo, Japan.
SOURCE: Respiration and Circulation, (1995) Vol. 43, No. 3, pp. 293-296.
ISSN: 0452-3458 CODEN: KOJUA9
COUNTRY: Japan

DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
031 Arthritis and Rheumatism
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: Japanese
SUMMARY LANGUAGE: Japanese; English
ENTRY DATE: Entered STN: 20 Apr 1995
Last Updated on STN: 20 Apr 1995

AB A patient with protein-losing enteropathy (PLE) associated with mixed connective tissue disease (MCTD), who developed superior vena cava thrombosis is described. A 51-year-old woman was admitted to our hospital because of generalized edema. She showed strong facial edema on the right side. Serum albumin level and antithrombin III (AT III) activities were markedly decreased. Venous angiography showed a thrombus of the superior vena cava. Neither liver dysfunction nor nephrotic syndrome was present. After an elevation of 24-hour fecal . alpha.(1) anti-trypsin clearance, and abdominal scintigraphy, following intravenous injection of (99m)Tc-human serum albumin D(HSAD), radioactivity in the intestine was observed, we confirmed that PLE was the main etiology of her hypoproteinemia. Only anti-U1 ribonucleoprotein (RNP) antibody was positive, although the titer was low. The case was suspected MCTD and corticosteroid pulse therapy followed by the oral administration of 20 mg prednisolone (PSL) a day was performed. Within one week, there was a rise in the serum albumin level and AT III activity. Finally 5 mg oral administration of PSL alone was enough to maintain normal serum albumin level and AT III activity. Abdominal scintigraphy of (99m)Tc-HSAD clearly demonstrated a decrease in radioactivity. Severe hypoproteinemia due to leakage of plasma proteins into the intestinal lumen may be related to a decrease in the blood levels of anticoagulation factors and the formation of thrombi in the vessels. Decreased AT III activity is well known for its tendency to be accompanied by thrombi formation in hereditary cases of AT III deficiency. AT III is the most important anticoagulation factor, and we should consider thrombosis in its relation to other acquired protein-losing diseases.

L18 ANSWER 11 OF 29 BIOTECHDS COPYRIGHT 2009 THOMSON REUTERS on STN
ACCESSION NUMBER: 1995-15151 BIOTECHDS Full-text
TITLE: Gene therapy using liposome vectors; mouse tumor necrosis factor and human alpha-1-antitrypsin gene transfer by lipofection for enzyme deficiency and cancer cytokine-mediated gene therapy (conference abstract)
AUTHOR: Alino S F
CORPORATE SOURCE: Univ.Valencia
LOCATION: Departmento de Farmacologia, Facultat de Medicina, Universitat de Valencia, Av. Blasco Ibanez, 15. 46010-Valencia, Spain.
SOURCE: Methods Find.Exp.Clin.Pharmacol.; (1995) 17, Suppl.A, 15-16
CODEN: MFEPDX
ISSN: 0379-0355
XIX National Meeting of the Spanish Society of Pharmacology, Madrid, Spain, 4-6 October, 1995.
DOCUMENT TYPE: Journal
LANGUAGE: English
AN 1995-15151 BIOTECHDS Full-text
AB The in vivo use of gene therapy requires the development of delivery vectors, e.g. liposomes, for in vivo gene transfer. The nucleic acid can be situated

on the outer liposome surface by electrostatic interactions between negatively charged phosphate groups of the nucleic acid and positively charged lipids. The cationic lipid subsequently facilitates gene delivery by liposome transfer with the cell membrane. This procedure was utilized for a cancer gene therapy strategy employing plasmid pNBT containing 0.3 kb beta-actin promoter and 0.7 kb mouse tumor necrosis factor (TNF) cDNA. Results indicated that TNF gene therapy induced tumor growth inhibition. Alternatively, the nucleic acid can be encapsulated into liposomes in order to protect it from nuclease digestion after i.v. administration. This was utilized to mediate delivery of a human alpha- 1-antitrypsin gene, bearing its own promoter, to mouse hepatocytes in vivo. The best results were obtained when small anionic liposomes targeted at asialoglycoprotein receptors were employed. (0 ref)

L18 ANSWER 12 OF 29 WPIX COPYRIGHT 2009 THOMSON REUTERS on STN
ACCESSION NUMBER: 1994-134077 [16] WPIX
CROSS REFERENCE: 1993-075758
DOC. NO. CPI: C1994-062140 [16]
TITLE: Novel saccharin-methyl derivs. inhibit protease enzymes - are di:ethyl-4-isopropyl -6-methoxy-2-saccharinyl-methyl phosphate
DERWENT CLASS: B02
INVENTOR: COURT J J; DESAI R C; HLASTA D J
PATENT ASSIGNEE: (SNFI-C) SANOFI; (STER-C) STERLING WINTHROP INC
COUNTRY COUNT: 23

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 5296496	A	19940322	(199416)*	EN	31[0]	
EP 601623	A1	19940615	(199423)	EN	22[0]	
AU 9350583	A	19940623	(199430)	EN		
CA 2102592	A	19940609	(199434)	EN		
JP 06228177	A	19940816	(199437)	JA	7[0]	
AU 670635	B	19960725	(199637)	EN		
HU 70747	T	19951030	(199732)	HU		
SG 50603	A1	19980720	(199838)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5296496	A CIP of	US 1991-814741	19911227

US 5296496 A	US 1992-988424 19921208
CA 2102592 A	CA 1993-2102592 19931105
AU 9350583 A	AU 1993-50583 19931110
AU 670635 B	AU 1993-50583 19931110
EP 601623 A1	EP 1993-203240 19931118
JP 06228177 A	JP 1993-290600 19931119
HU 70747 T	HU 1993-3318 19931123
SG 50603 A1	SG 1996-6222 19931118

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 5296496 A	CIP of	US 5187173 A
AU 670635 B	Previous Publ	AU 9350583 A

PRIORITY APPLN. INFO: US 1992-988424 19921208
US 1991-814741 19911227

AN 1994-134077 [16] WPIX
CR 1993-075758
AB US 5296496 A UPAB: 20050507
Saccharinyl-methyl derivs. of formula (I) and their salts are new; R1 = H, halo, lower alkyl, perfluoro (lower alkyl), etc.; R2, R3 = H or in any available 5, 6 or 7 positions a halo, CN, NO2; m,n = 0 or 1; A, B (when m and n = 1) = H, lower alkyl, phenyl etc.; A, B (when m = 1 and n = 0) = lower alkyl, phenyl, benzyl or 2-pyridinyl; A, B (when m and n = 0) = lower alkyl, phenyl or lower alkoxyphenyl. Diethyl 4-isopropyl-6-methoxy-2-saccharinyl-methyl phosphate is specifically claimed.
USE - (I) inhibit the activity of protease enzymes especially serine proteases, specifically human leukocyte elastase and the chymotrypsin-like enzymes, and thus are useful in the treatment of degenerative diseases such as emphysema, rheumatoid arthritis, pancreatitis, cystic fibrosis, chronic bronchitis, adult respiratory distress syndrome, inflammatory bowel disease, psoriasis, bullous pemphigus and alpha-1- anti-trypsin deficiency. (I) can be administered orally, parenterally or by aerosol inhalation.

L18 ANSWER 13 OF 29 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 1994236998 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8181327
TITLE: Replacement therapy for hereditary alpha1-antitrypsin deficiency. A program for long-term administration.
AUTHOR: Barker A F; Siemsen F; Pasley D; D'Silva R; Buist A S
CORPORATE SOURCE: Department of Pulmonary and Critical Care Medicine, Oregon Health Sciences University, Portland.
SOURCE: Chest, (1994 May) Vol. 105, No. 5, pp. 1406-10.
Journal code: 0231335. ISSN: 0012-3692.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199406
ENTRY DATE: Entered STN: 21 Jun 1994
Last Updated on STN: 9 May 2002
Entered Medline: 15 Jun 1994
AB This retrospective chart review describes the efficacy and safety of long-term administration of intravenous alpha1-antitrypsin (AAT) in 14 patients with hereditary AAT deficiency and COPD. During the 12- to 48-month observation

period, 12 to 14 patients had stabilization of functional status; 4 patients had reductions in hospitalizations. Thirteen of 14 patients had no decline in pulmonary function. Three patients had self-limited adverse reactions to the AAT with one patient requiring a brief hospitalization.

L18 ANSWER 14 OF 29 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 1995147374 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 7844913
TITLE: Effect of E. coli endotoxin and D-galactosamine on pathophysiology in rat lungs.
AUTHOR: Aritomi T; Yoshida M; Toyoshima H; Takihara H; Ishibashi M; Watanabe K
CORPORATE SOURCE: Second Department of Internal Medicine, School of Medicine, Fukuoka University.
SOURCE: Nihon Kyobu Shikkan Gakkai zasshi, {1994 Oct} Vol. 32, No. 10, pp. 956-62.
Journal code: 7505737. ISSN: 0301-1542.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 16 Mar 1995
Last Updated on STN: 3 Mar 2000
Entered Medline: 7 Mar 1995

AB The effects of repeated intravenous injection of E. coli endotoxin (ETX) and intraperitoneal injection of D-galactosamine (GAL), which decreases the circulating level of alpha 1-antitrypsin, on the pathophysiology of chronic lung injury was studied in rats. Four groups were prepared as follows for 8 weeks. Group 1 (control): Intravenous injection of saline. Group 2: Intravenous injection of ETX (2 mg/kg) once a week. Group 3: Intraperitoneal injection of GAL (200 mg/kg), 2 times daily on 3 consecutive days each week. Group 4: Injection of both ETX and GAL, at the same dosages as used in groups 2 and 3. Total lung capacity and static lung compliance divided by weight were high in the ETX group and the ETX + GAL group, comparative when compared with those in the control and GAL groups, even though weight gain rates in the ETX + GAL group was less than in other groups. Mean linear intercept of rats in the ETX + GAL group was significantly greater than in other groups. These results suggest that ETX + GAL-treated rats have more emphysematous changes in pulmonary function and structure.

L18 ANSWER 15 OF 29 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 1995050032 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 7961263
TITLE: No lung toxicity after repeated aerosol or intravenous delivery of plasmid-cationic liposome complexes.
AUTHOR: Canonico A E; Plitman J D; Conary J T; Meyrick B O; Brigham K L
CORPORATE SOURCE: Department of Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee 37232.
CONTRACT NUMBER: HL-07123 (United States NHLBI NIH HHS)
HL-19153 (United States NHLBI NIH HHS)
HL-45151 (United States NHLBI NIH HHS)
SOURCE: Journal of applied physiology (Bethesda, Md. : 1985), {1994 Jul} Vol. 77, No. 1, pp. 415-9.
Journal code: 8502536. ISSN: 8750-7587.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 10 Jan 1995
Last Updated on STN: 10 Jan 1995
Entered Medline: 12 Dec 1994

AB The safety aspects of human gene therapy are of paramount importance in developing an ideal system for gene transfer. Lipofection using DNA in the form of a plasmid has been shown to successfully transfect the lungs when administered either intravenously or by aerosol. We have shown that repeated intravenous or aerosol administration of a plasmid containing the recombinant human alpha 1- antitrypsin gene and a cytomegalovirus promoter complexed to cationic liposomes results in no adverse effects on pulmonary histology, lung compliance, lung resistance, or alveolar-arterial oxygen gradient. Immunohistochemistry and Western blot analysis confirm successful gene transfer using this delivery system. We conclude that plasmids complexed to cationic liposomes may be a safe and efficacious delivery system for in vivo gene transfer to the lungs. Using this delivery system, in vivo gene therapy to the lungs can be achieved by either intravenous or aerosol administration of the transgene.

L18 ANSWER 16 OF 29 BIOTECHDS COPYRIGHT 2009 THOMSON REUTERS on STN
ACCESSION NUMBER: 1994-12255 BIOTECHDS Full-text
TITLE: No lung toxicity after repeated aerosol or intravenous delivery of plasmid-cationic liposome complexes; human alpha-1-antitrypsin gene transmission to lung by lipofection as a means of lung disease gene therapy
AUTHOR: Cononico A E; Plitman J D; Conary J T; Meyrick B O; Brigham K L
CORPORATE SOURCE: Univ.Vanderbilt
LOCATION: Center for Lung Research, Departments of Medicine and Pathology, Vanderbilt University School of Medicine, Nashville, Tennessee 37232, USA.
SOURCE: J.Appl.Physiol.; (1994) 77, 1, 415-19
CODEN: 5119T
DOCUMENT TYPE: Journal
LANGUAGE: English
AN 1994-12255 BIOTECHDS Full-text
AB The safety aspects of human gene therapy are of paramount importance in developing an ideal system for gene transfer. Lipofection using DNA in the form of a plasmid has been shown to successfully transfect the lungs when administered either i .v. or by aerosol. Repeated i.v. or aerosol administration of plasmid pCMV4-alpha-1-AT containing the human recombinant alpha-1- antitrypsin gene and a cytomegalo virus promoter complexed to cationic liposomes to New Zealand White rabbits resulted in no adverse effects on pulmonary histology, lung compliance, lung resistance or alveolar-arterial oxygen gradient. Sustained levels of transgene-directed protein biosynthesis was demonstrated over a 4-wk period. Immunohistochemistry and Western blot analysis confirmed successful gene transmission using this delivery system. It was concluded that plasmids complexed to cationic liposomes may be a safe and efficacious delivery system for in vivo gene transfer to the lungs. Using this delivery system, in vivo gene therapy to the lungs can be achieved by either i.v. or aerosol administration of the transgene. (23 ref)

L18 ANSWER 17 OF 29 BIOTECHDS COPYRIGHT 2009 THOMSON REUTERS on STN
ACCESSION NUMBER: 1995-07701 BIOTECHDS Full-text
TITLE: Hepatic gene therapy strategies in vivo, using small liposomes;
alpha-1-antitrypsin gene expression in mouse liver using plasmid pTG7101 in liposome, for application in liver disease gene therapy (conference abstract)
AUTHOR: Crespo J; Blaya C; Crespo A; Escrig E; Alino S F
CORPORATE SOURCE: Univ.Valencia
LOCATION: Departamento de Farmacologia, Fac. Medicina, Univ. Valencia, Valencia 46010, Spain.
SOURCE: Methods Find.Exp.Clin.Pharmacol.; (1994) 16, Suppl.1, 66
CODEN: MFEPDX
ISSN: 0379-0355
XVIII National Meeting of the Spanish Society of Pharmacology, Alicante, Spain, 2-4 November, 1994.
DOCUMENT TYPE: Journal
LANGUAGE: English
AN 1995-07701 BIOTECHDS Full-text
AB Small liposomes were used for in vivo hepatic disease gene therapy of alpha-1-antitrypsin deficiency. I.v. injection of liposomes harboring plasmid pTG7101 (containing the human alpha-1-antitrypsin gene) induced expression of human protein in the mouse liver. Hepatocytes were the main targets for small liposomes (diameter less than 100 nm) whereas Kupffer cells were probably the main target for large liposomes. Groups were treated (100 ng/mouse) with repetitive doses (days 0, 3, 7 and 10) or with a single dose (day 0) plus partial hepatectomy. The human protein was detected (16 ng/ml) in all cases, from the 1st dose. The repetitive dose treatment did not produce an additive effect on protein expression. The single dose plus partial hepatectomy increased the plasma levels of the human protein 1-to 10-fold. (1 ref)

L18 ANSWER 18 OF 29 WPIX COPYRIGHT 2009 THOMSON REUTERS on STN
ACCESSION NUMBER: 1993-160862 [20] WPIX
CROSS REFERENCE: 1990-361410; 1992-152592; 1992-249450; 1993-160863; 1993-344358; 1994-134787; 1996-229899; 1997-108360
DOC. NO. CPI: C1993-071003 [21]
TITLE: New saccharin derivs. are proteolytic enzyme inhibitors - for treating degenerative disorders e.g. emphysema, rheumatoid arthritis, pancreatitis
DERWENT CLASS: B02
INVENTOR: DESAI P C; DESAI R; DESAI R C; DUNLAP R P; HLASTA D J; LATIMER L; LATIMER L H; MURA A A; MURA A J; SUBRAMANYAM C
PATENT ASSIGNEE: (SNFI-C) SANOFI; (SNFI-C) SANOFI SA; (STER-C) STERLING WINTHROP INC
COUNTRY COUNT: 30

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
EP 542371	A1	19930519	(199320)*	EN	17[0]	

```
      <--
                                                        <--
      AU 9226057      A  19930520 (199327)  EN
      <--
                                                        <--
      NO 9204402      A  19930518 (199328)  NO
      <--
                                                        <--
      FI 9205166      A  19930516 (199330)  FI
      <--
                                                        <--
      CA 2082774      A  19930516 (199332)  EN
      <--
                                                        <--
      CZ 9203388      A3 19930616 (199338)  CS
      <--
                                                        <--
      JP 06122675     A  19940506 (199423)  JA  15[0]
      <--
                                                        <--
      HU 65694        T  19940728 (199431)  HU
      <--
                                                        <--
      US 5380737      A  19950110 (199508)  EN  12[0]
      <--
                                                        <--
      AU 656027       B  19950119 (199510)  EN
      <--
                                                        <--
      US 5464852      A  19951107 (199550)  EN  11[0]
      <--
                                                        <--
      NZ 245126       A  19960126 (199610)  EN
      <--
                                                        <--
      TW 282463       A  19960801 (199649)  ZH
      <--
                                                        <--
      US 5578623      A  19961126 (199702)  EN  11[0]
      <--
                                                        <--
      NO 302887       B1 19980504 (199825)  NO
      <--
                                                        <--
      US 5773456      A  19980630 (199833)  EN
      <--
                                                        <--
      IL 103747       A  19980615 (199836)  EN
      <--
                                                        <--
      SG 52778        A1 19980928 (199904)  EN
      <--
                                                        <--
      RU 2114835      C1 19980710 (200001)  RU
      <--

APPLICATION DETAILS:

      PATENT NO      KIND                 APPLICATION    DATE
      ----------------------------------------------------------------------
```

EP 542371 A1	EP 1992-203468 19921112
US 5380737 A CIP of	US 1989-347125 19890504
US 5464852 A CIP of	US 1989-347125 19890504
US 5578623 A CIP of	US 1989-347125 19890504
US 5773456 A CIP of	US 1989-347125 19890504
US 5380737 A CIP of	US 1989-347126 19890504
US 5464852 A CIP of	US 1989-347126 19890504
US 5578623 A CIP of	US 1989-347126 19890504
US 5773456 A CIP of	US 1989-347126 19890504
US 5380737 A CIP of	US 1990-514920 19900426
US 5464852 A CIP of	US 1990-514920 19900426
US 5578623 A CIP of	US 1990-514920 19900426
US 5773456 A CIP of	US 1990-514920 19900426
US 5380737 A CIP of	US 1990-608068 19901101
US 5464852 A CIP of	US 1990-608068 19901101
US 5578623 A CIP of	US 1990-608068 19901101
US 5773456 A CIP of	US 1990-608068 19901101
US 5380737 A CIP of	US 1991-782016 19911024
US 5464852 A CIP of	US 1991-782016 19911024
US 5578623 A CIP of	US 1991-782016 19911024
US 5773456 A CIP of	US 1991-782016 19911024
US 5380737 A Cont of	US 1991-793035 19911115
US 5464852 A Cont of	US 1991-793035 19911115
US 5578623 A Cont of	US 1991-793035 19911115
US 5773456 A Cont of	US 1991-793035 19911115
AU 9226057 A	AU 1992-26057 19920930
AU 656027 B	AU 1992-26057 19920930
TW 282463 A	TW 1992-107772 19920930
CA 2082774 A	CA 1992-2082774 19921112
CZ 9203388 A3	CS 1992-3388 19921113
FI 9205166 A	FI 1992-5166 19921113
HU 65694 T	HU 1992-3561 19921113
IL 103747 A	IL 1992-103747 19921113
NO 9204402 A	NO 1992-4402 19921113
NO 302887 B1	NO 1992-4402 19921113
NZ 245126 A	NZ 1992-245126 19921113
RU 2114835 C1	RU 1992-4409 19921113
JP 06122675 A	JP 1992-305222 19921116
US 5380737 A	US 1993-113508 19930827
US 5464852 A Div Ex	US 1993-113508 19930827
US 5578623 A Div Ex	US 1993-113508 19930827
US 5773456 A Div Ex	US 1993-113508 19930827
US 5464852 A	US 1994-289113 19940811
US 5578623 A Div Ex	US 1994-289113 19940811
US 5773456 A Div Ex	US 1994-289113 19940811
US 5578623 A	US 1995-445240 19950519
US 5773456 A Div Ex	US 1995-445240 19950519
SG 52778 A1	SG 1996-9394 19921112
US 5773456 A	US 1996-719216 19960925

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 656027 B	Previous Publ	AU 9226057 A
NO 302887 B1	Previous Publ	NO 9204402 A
US 5380737 A	CIP of	US 5128339 A
US 5464852 A	CIP of	US 5128339 A
US 5578623 A	CIP of	US 5128339 A
US 5773456 A	CIP of	US 5128339 A

US 5464852 A	Div ex	US 5380737 A
US 5578623 A	Div ex	US 5380737 A
US 5773456 A	Div ex	US 5380737 A
US 5578623 A	Div ex	US 5464852 A
US 5773456 A	Div ex	US 5464852 A
US 5773456 A	Div ex	US 5578623 A

PRIORITY APPLN. INFO: US 1991-793035 19911115
US 1989-347125 19890504
US 1989-347126 19890504
US 1990-514920 19900426
US 1990-608068 19901101
US 1991-782016 19911024
US 1993-113508 19930827
US 1994-289113 19940811
US 1995-445240 19950519
US 1996-719216 19960925

AN 1993-160862 [20] WPIX

CR 1990-361410; 1992-152592; 1992-249450; 1993-160863; 1993-344358; 1994-134787; 1996-229899; 1997-108360

AB EP 542371 A1 UPAB: 20050509
Saccharin derivs. of formula (I) and their salts are new. In (I) L = NO, O or SOn; n = 0, 1 or 2; L-R1 is a leaving gp., H-L-R1 is the conjugate acid thereof and, when L=N, H-l-R1 has Pka upto 6, when L=O, H-L-R1, has pka upto 8 and when l = SOn, H-L-R1 has pka upto 5; R2 = prim or sec. 2-4C alkyl, prim. 1-3C alkylamino, prim. 2-4C alkyl-methylamino, diethylamino or prim. 1-3C alkoxy; R3 = H, lower alkyl, cycloalkyl, amino lower alkyl, lower alkylamino lower alkyl, di-lower alkylamino - lower alkyl, hydroxy lower alkyl, lower alkoxy lower alkyl, perfluoro lower alkyl, perchloro lower alkyl, CHO, CN, CO2H, aminocarbonyl, R-oxycarbonyl, B = N, 1- lower alkyl-2-pyrrolyl, lower alkyl sulphonylamino, perfluoro lower alkylsulphonylamino, perchloro lower alkyl sulphonylamino, NO2, OH, lower alkoxy, cycloalkoxy, B = N - lower alkoxy, hydroxy lower alkoxy, polyhydroxy lower alkoxy or acetal or ketal thereof, lower alkoxy lower alkoxy, poly-lower alkoxy-lower alkoxy, hydroxy-poly lower alkyleneoxy, lower alkoxy- poly- lower alkyleneoxy, B = N-carbonyloxy, carboxy lower alkoxy, R-oxycarbonyl lower alkoxy, methylene-dioxy, di-lower alkyl phosphonyloxy, R-thio, R-sulphinyl, R-sulphonyl, perfluoro - lower alkylsulphonyl, perchloro-lower alkylsulphonyl, aminosulphonyl, lower alkylaminosulphonyl, di-lower alkylaminosulphonyl or halo; m = 1-3; B=N = amino, mono-or di-lower alkylamino, carboxy lower-alkylamino, 1-pyrrolidinyl, 1-piperdinyl, 1-azetidinyl, 4- morpholinyl, 1-piperazinyl, 4-lower alkyl-1- piperazinyl, 4-benzyl- -1 piperazinyl or 1-imidazolyl; R = lower alkyl, benzyl or phenyl or naphthyl opt. substd. by 1 or 2 of lower alkyl, lower alkoxy or halo.
USE - (I) are proteolytic enzyme inhibitors and are useful in the treatment of degenerative diseases e.g. emphysema, rheumatoid arthritis, pancreatitis, cystic fibrosis, chronic bronchitis, adult respiratory distress syndrome, inflammatory bowel disease, psoriasis, bullous pernphigoid and alpha-1 - antitrypsin deficiency. Admin. may be oral, parenteral or by aerosol inhalation. - .D

Member(0009)

ABEQ US 5380737 A UPAB 20050509
Treatment comprises administering a proteolytic enzyme inhibiting amt of a cpd of formula (I), where L is N; L-R1 is N-heterocyclyl leaving gp; and H-L-R1 is its conjugate acid of pKa less than or equal to 6; R2 is prim or sec alkyl of 2-4C, 1-3C prim alkylamino, 2-4C prim alkylmethylamino or 1-3C diethylamino or prim alkoxy; R3 is 1-3 specified substits at any or all of the 5-, 6- or

7-positions.
USE - The cpds inhibit the enzymatic activity of proteolytic enzymes in the treatment of degenerative diseases. Admin is by oral, parenteral or aerosol inhalation in solid or liquid as tablets, capsules, solns, suspensions and emulsions. Dosage is dependent on the individual patients' criteria.

Member(0011)
ABEQ US 5464852 A UPAB 20050509
Saccharin derivs. of formula (I) and their salts are new. In the formula, L-R1 is opt. substd. triazolyl; R2 is prim. or sec. 2-4C alkyl, prim.- 1-3C alkylamino, and - 2-4C alkylmethylamino, diethylamino or 1-3C alkoxy; R3 is 1-3 substits. at any or all of 5-, 6- and 7-positions being H, lower alkyl, cycloalkyl, aminoalkyl, alkylaminoalkyl, di-alkylaminoalkyl, OHalkyl, alkoxyalkyl, perfluoro- and perchloro-alkyl, formyl, CN, COO, etc.
2-(4,5-di(t-butylsulphonyl) -1,2,3-triazol-1-yl)methyl-4- isopropyl -6-methoxysaccharin is specifically claimed.
USE - (I) inhibit proteolytic enzymes and compsns. are used in treatment of degenerative diseases, including emphysema, rheumatoid arthritis and pancreatitis.

Member(0016)
ABEQ US 5773456 A UPAB 20050509
Saccharin derivs. of formula (I) and their salts are new. In (I) L = NO, O or SOn; n = 0, 1 or 2; L-R1 is a leaving gp., H-L-R1 is the conjugate acid thereof and, when L=N, H-l-R1 has Pka upto 6, when L=O, H-L-R1, has pka upto 8 and when l = SOn, H-L-R1 has pka upto 5; R2 = prim or sec. 2-4C alkyl, prim. 1-3C alkylamino, prim. 2-4C alkyl-methylamino, diethylamino or prim. 1-3C alkoxy; R3 = H, lower alkyl, cycloalkyl, amino lower alkyl, lower alkylamino lower alkyl, di-lower alkylamino - lower alkyl, hydroxy lower alkyl, lower alkoxy lower alkyl, perfluoro lower alkyl, perchloro lower alkyl, CHO, CN, CO2H, aminocarbonyl, R-oxycarbonyl, B = N, 1- lower alkyl-2-pyrrolyl, lower alkyl sulphonylamino, perfluoro lower alkylsulphonylamino, perchloro lower alkyl sulphonylamino, NO2, OH, lower alkoxy, cycloalkoxy, B = N - lower alkoxy, hydroxy lower alkoxy, polyhydroxy lower alkoxy or acetal or ketal thereof, lower alkoxy lower alkoxy, poly-lower alkoxy-lower alkoxy, hydroxy-poly lower alkyleneoxy, lower alkoxy- poly- lower alkyleneoxy, B = N-carbonyloxy, carboxy lower alkoxy, R-oxycarbonyl lower alkoxy, methylene-dioxy, di-lower alkyl phosphonyloxy, R-thio, R-sulphinyl, R-sulphonyl, perfluoro - lower alkylsulphonyl, perchloro-lower alkylsulphonyl, aminosulphonyl, lower alkylaminosulphonyl, di-lower alkylaminosulphonyl or halo; m = 1-3; B=N = amino, mono-or di-lower alkylamino, carboxy lower-alkylamino, 1-pyrrolidinyl, 1-piperdinyl, 1-azetidinyl, 4- morpholinyl, 1-piperazinyl, 4-lower alkyl-1- piperazinyl, 4-benzyl- -1 piperazinyl or 1-imidazolyl; R = lower alkyl, benzyl or phenyl or naphthyl opt. substd. by 1 or 2 of lower alkyl, lower alkoxy or halo.
USE - (I) are proteolytic enzyme inhibitors and are useful in the treatment of degenerative diseases e.g. emphysema, rheumatoid arthritis, pancreatitis, cystic fibrosis, chronic bronchitis, adult respiratory distress syndrome, inflammatory bowel disease, psoriasis, bullous pernphigoid and alpha-1 -antitrypsin deficiency. Admin. may be oral, parenteral or by aerosol inhalation. - .D

Member(0019)
ABEQ RU 2114835 C1 UPAB 20050509
Saccharin derivs. of formula (I) and their salts are new. In (I) L =

NO, O or SOn; n = 0, 1 or 2; L-R1 is a leaving gp., H-L-R1 is the conjugate acid thereof and, when L=N, H-l-R1 has Pka upto 6, when L=O, H-L-R1, has pka upto 8 and when l = SOn, H-L-R1 has pka upto 5; R2 = prim or sec. 2-4C alkyl, prim. 1-3C alkylamino, prim. 2-4C alkyl-methylamino, diethylamino or prim. 1-3C alkoxy; R3 = H, lower alkyl, cycloalkyl, amino lower alkyl, lower alkylamino lower alkyl, di-lower alkylamino - lower alkyl, hydroxy lower alkyl, lower alkoxy lower alkyl, perfluoro lower alkyl, perchloro lower alkyl, CHO, CN, CO2H, aminocarbonyl, R-oxycarbonyl, B = N, 1- lower alkyl-2-pyrrolyl, lower alkyl sulphonylamino, perfluoro lower alkylsulphonylamino, perchloro lower alkyl sulphonylamino, NO2, OH, lower alkoxy, cycloalkoxy, B = N - lower alkoxy, hydroxy lower alkoxy, polyhydroxy lower alkoxy or acetal or ketal thereof, lower alkoxy lower alkoxy, poly-lower alkoxy-lower alkoxy, hydroxy-poly lower alkyleneoxy, lower alkoxy- poly- lower alkyleneoxy, B = N-carbonyloxy, carboxy lower alkoxy, R-oxycarbonyl lower alkoxy, methylene-dioxy, di-lower alkyl phosphonyloxy, R-thio, R-sulphinyl, R-sulphonyl, perfluoro - lower alkylsulphonyl, perchloro-lower alkylsulphonyl, aminosulphonyl, lower alkylaminosulphonyl, di-lower alkylaminosulphonyl or halo; m = 1-3; B=N = amino, mono-or di-lower alkylamino, carboxy lower-alkylamino, 1-pyrrolidinyl, 1-piperdinyl, 1-azetidinyl, 4- morpholinyl, 1-piperazinyl, 4-lower alkyl-1- piperazinyl, 4-benzyl- -1 piperazinyl or 1-imidazolyl; R = lower alkyl, benzyl or phenyl or naphthyl opt. substd. by 1 or 2 of lower alkyl, lower alkoxy or halo.

USE - (I) are proteolytic enzyme inhibitors and are useful in the treatment of degenerative diseases e.g. emphysema, rheumatoid arthritis, pancreatitis, cystic fibrosis, chronic bronchitis, adult respiratory distress syndrome, inflammatory bowel disease, psoriasis, bullous pernphigoid and alpha-1 -antitrypsin deficiency. Admin. may be oral, parenteral or by aerosol inhalation. - .D

L18 ANSWER 19 OF 29 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 1994169920 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8124298
TITLE: Studies on lymphocyte characteristics in patients with homozygous alpha 1-proteinase inhibitor deficiency during substitution therapy.
AUTHOR: Schoenfeld N; Schmitt M; Remy N; Wahn U; Loddenkemper R
CORPORATE SOURCE: Dept of Pulmonary Medicine II, Chest Hospital Heckeshorn, Berlin, Germany.
SOURCE: Monaldi archives for chest disease = Archivio Monaldi per le malattie del torace / Fondazione clinica del lavoro, IRCCS [and] Istituto di clinica tisiologica e malattie apparato respiratorio, Universita di Napoli, Secondo ateneo, (1993 Dec) Vol. 48, No. 6, pp. 613-6.
Journal code: 9307314. ISSN: 1122-0643.
PUB. COUNTRY: Italy
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199404
ENTRY DATE: Entered STN: 20 Apr 1994
Last Updated on STN: 3 Feb 1997
Entered Medline: 13 Apr 1994

AB Alpha 1-proteinase inhibitor (alpha 1-PI) has been demonstrated to suppress mitogen-induced lymphocyte response in vitro. To evaluate the effect of intravenous application of human alpha 1-PI (Prolastin HS) on cellular immunity, we determined total lymphocyte count, lymphocyte subsets and

lymphocyte response to concanavalin A, before and 24 h after infusion of 60 mg.kg-1 body weight alpha 1-PI in eight patients with homozygous alpha 1-PI deficiency (PiZ phenotype). The results were compared with two blood samples from seven healthy controls. After infusion, serum alpha 1-PI levels were increased from 0.98 +/- 0.24 to 2.68 +/- 0.51 g.l-1. No significant differences were found for total lymphocyte count, lymphocyte subsets and lymphocyte response between both groups in both samples. Maximum 3H-thymidine incorporation before and after infusion showed no significant difference; the same was true for the two control samples. However, additional incubation in vitro with alpha 1-PI 5 g.l-1 led to a significant ($p < 0.03$) decrease of lymphocyte proliferation in samples after infusion. Our data indicate that alpha 1-PI substitution therapy does not lead to a major suppression of lymphocyte response to concanavalin A in PiZ individuals in vivo, although a suppressive effect was found after additional in vitro incubation with alpha 1-PI.

L18 ANSWER 20 OF 29 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 1993362590 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8356934
TITLE: Alpha 1-antitrypsin augmentation therapy.
AUTHOR: Sandhaus R A
CORPORATE SOURCE: Swedish Hospital, Denver, CO.
SOURCE: Agents and actions. Supplements, (1993) Vol. 42, pp. 97-102. Ref: 14
Journal code: 7801014. ISSN: 0379-0363.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199309
ENTRY DATE: Entered STN: 8 Oct 1993
Last Updated on STN: 8 Oct 1993
Entered Medline: 21 Sep 1993

AB Alpha 1-proteinase inhibitor (also known as alpha 1-antitrypsin) derived from pooled human serum (Prolastin, Miles Biologicals) has been available in the United States since 1988. Although no formal controlled prospective study has been performed to prove its efficacy, intravenous administration of Prolastin has been the accepted treatment for individuals with pulmonary emphysema due to alpha 1-antitrypsin deficiency. In addition, Prolastin has been used experimentally by inhalation for the treatment of cystic fibrosis. It has been administered with some success to treat the panniculitis associated with alpha 1-antitrypsin deficiency. As a greater number of severely impaired alpha 1-antitrypsin deficient patients receive lung transplantation, the role of Prolastin in the post-transplant therapy of these patients will need evaluation. Newer antiproteases may render Prolastin obsolete with respect to its route of administration and its pricing, however, the safety record of this drug has been impressive.

L18 ANSWER 21 OF 29 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 1991025122 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2222515
TITLE: In vivo evidence for protease-catalysed mechanism providing bioactive tumor necrosis factor alpha.
AUTHOR: Niehorster M; Tiegs G; Schade U F; Wendel A
CORPORATE SOURCE: Faculty of Biology, University of Konstanz, Federal Republic of Germany.
SOURCE: Biochemical pharmacology, (1990 Oct 1) Vol.

40, No. 7, pp. 1601-3.
Journal code: 0101032. ISSN: 0006-2952.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199011
ENTRY DATE: Entered STN: 17 Jan 1991
Last Updated on STN: 3 Mar 2000
Entered Medline: 8 Nov 1990

AB Mice pretreated by intravenous injection of 42 mg/kg of the serine protease inhibitor alpha 1-antitrypsin prior to a hepatotoxic dose of D-galactosamine/lipopolysaccharide (GalN/LPS) were fully protected against hepatitis. Pretreatment with alpha 1-antitrypsin with doses up to 300 mg/kg at different times failed to protect galactosamine sensitized animals against tumor necrosis factor alpha (TNF alpha)-induced hepatitis. No bioactive TNF alpha was detectable in serum of mice protected against GalN/LPS-induced hepatitis by pretreatment with alpha 1-antitrypsin. In contrast, abundant amounts of TNF were found in sera of GalN/LPS-treated control animals. It is concluded that a serine protease sensitive to alpha 1-antitrypsin provides bioactive TNF alpha by proteolytic cleavage of a TNF alpha precursor.

L18 ANSWER 22 OF 29 PROMT COPYRIGHT 2009 Gale Group on STN

ACCESSION NUMBER: 90:424266 PROMT Full-text
TITLE: CarePlus - Acquisitions & Mergers
SOURCE: Annual Report, (1989) pp. 0.
LANGUAGE: English

AB During 1989 we acquired Home Parenteral Services, a leading home infusion provider in Kansas City. We also expanded into Raleigh/Durham, North Carolina. In January of 1990, we completed the acquisition of Home Nutritional Systems of Oakland, California. We expect to continue this growth pattern with the opening of two to three more markets in 1990. In addition to this new market expansion, our growth has been fueled by increased sales in our existing offices and by the introduction of new therapies. In 1989, CarePlus was the first company to offer home administration of erythropoietin for anemias related to chronic renal failure. The introduction of new therapies such as home blood products administration , I.V. Prolastin, deferoxamine, human growth hormone, and now erythropoietin, has solidified CarePLus' position as a clinical leader in the home infusion therapy field.
As CarePlus continues to grow and evolve, the one basic principle that will never change is our firm commitment to provide the highest quality of care available. Every aspect of our program meets or exceeds the new homecare standards of the Joint Commission on Accreditation of Healthcare Organizations. Our exhaustive Quality Assurance Program includes 14 major audits of over 275 individual criteria, and involves a clinical review of every patient we serve. Combined with our Clinical Management Teams and various regional and national advisory boards, these programs help us ensure that as we grow we will maintain the unsurpassed quality of care that has become synonymous with CarePlus.

L18 ANSWER 23 OF 29 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1988:184470 BIOSIS Full-text
DOCUMENT NUMBER: PREV198885096572; BA85:96572
TITLE: BLOOD COAGULATION IN POSTMENOPAUSAL WOMEN GIVEN ESTROGEN TREATMENT COMPARISON OF TRANSDERMAL

AND ORAL ADMINISTRATION.
AUTHOR(S): ALKJAERSIG N [Reprint author]; FLETCHER A P; DE ZIEGLER D; STEINGOLD K A; MELDRUM D R; JUDD H L
CORPORATE SOURCE: VA MED CENT, GRECC, ST LOUIS, MO 63125, USA
SOURCE: Journal of Laboratory and Clinical Medicine, (1988) Vol. 111, No. 2, pp. 224-228.
CODEN: JLCMAK. ISSN: 0022-2143.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 11 Apr 1988
Last Updated on STN: 11 Apr 1988

AB The responses of the blood coagulation and related systems were studied in 23 postmenopausal women, all of whom received, in randomized order, therapy with conjugated oral estrogens (0.625 and 1.25 mg daily) and transdermally administered estradiol in doses of 25, 50, 100, and 200 µg/24 hr. Neither plasma fibrinopeptide A determinations nor plasma fibrinogen chromatographic findings were altered; thus there is no evidence of accelerated fibrinogen turnover with either form of therapy. However, . alpha.1-antitrypsin and plasminogen concentrations were significantly increased with higher dosage of oral but not with transdermally administered estrogen. Similarly, ceruloplasmin concentration was significantly elevated with both oral doses but was unchanged by transdermal therapy.

L18 ANSWER 24 OF 29 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 1988250272 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 3260074
TITLE: Intravenous administration of alpha-1-proteinase inhibitor in patients of PiZ and PiM phenotype. Preliminary report.
AUTHOR: Moser K M; Smith R M; Spragg R G; Tisi G M
CORPORATE SOURCE: Pulmonary and Critical Care Division, University of California, School of Medicine, San Diego.
SOURCE: The American journal of medicine, (1988 Jun 24) Vol. 84, No. 6A, pp. 70-4.
Journal code: 0267200. ISSN: 0002-9343.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198807
ENTRY DATE: Entered STN: 8 Mar 1990
Last Updated on STN: 8 Mar 1990
Entered Medline: 22 Jul 1988

AB Nine patients with moderate pulmonary emphysema, six of PiZ phenotype and three of PiM phenotype, have received a single intravenous infusion of alpha-1-proteinase inhibitor (human) (A1PI), in a dose of 60 mg/kg over a 30-minute period. They also received a tracer dose (300 microCi) of 131I-labeled A1PI. No active or passive immunization against hepatitis was given. No acute toxicity was observed. Compared with baseline data, significant elevations of serum A1PI (measured both antigenically and as anti-elastase activity) occurred, with a serum half-life approximating 110 hours. Bronchoalveolar lavage fluid, obtained 48 hours after infusion, reflected a significant increase in A1PI concentration versus baseline bronchoalveolar lavage fluid values. Serial gamma camera images of the lungs confirmed persistence of enhanced lung radioactivity for several days. Urinary desmosine excretion did not change following A1PI infusion. During the period of follow-up thus far,

no patient has had chronic toxicity, results of liver function tests have been stable, and there has been no development of hepatitis B antigen or antibodies to hepatitis B surface or core antigens.

L18 ANSWER 25 OF 29 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 1988250270 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 3289387
TITLE: Alpha-1-antitrypsin augmentation therapy for alpha-1-antitrypsin deficiency.
AUTHOR: Hubbard R C; Crystal R G
CORPORATE SOURCE: Pulmonary Branch, National Heart, Lung and Blood Institute, Bethesda, Maryland 20892.
SOURCE: The American journal of medicine, (1988 Jun 24) Vol. 84, No. 6A, pp. 52-62. Ref: 45
Journal code: 0267200. ISSN: 0002-9343.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198807
ENTRY DATE: Entered STN: 8 Mar 1990
Last Updated on STN: 3 Mar 2000
Entered Medline: 22 Jul 1988

AB Alpha-1-antitrypsin (A1AT) deficiency is a genetic disorder characterized by low serum levels of A1AT and a high risk for the development of emphysema. A1AT is the principal inhibitor of neutrophil elastase, such that a deficiency of A1AT results in insufficient anti-elastase protection in the lower respiratory tract, thus allowing neutrophil elastase to destroy alveolar structures. The goal of A1AT augmentation therapy in A1AT deficiency is to raise lung A1AT levels and anti-neutrophil elastase capacity to levels that will provide adequate protection against neutrophil elastase, thereby preventing the lung from further elastase-mediated degradation. Studies with intravenous administration of human A1AT (60 mg/kg at weekly intervals) demonstrate that serum A1AT levels increased from an average 33 +/- 8 mg/dl pre-infusion to a steady-state trough level of 117 +/- 4 mg/dl, well above the projected threshold protective serum level of A1AT. The infused A1AT diffused into the lung and significantly augmented the epithelial lining fluid A1AT levels, rising from an average 0.44 +/- 0.16 microM (pre-infusion) to 2.62 +/- 1.29 microM at the nadir level just prior to the next infusion. Of critical importance is the fact that the A1AT that diffused into the lung was active as an inhibitor or neutrophil elastase, resulting in significant augmentation of epithelial lining fluid anti-neutrophil elastase capacity and normalization of the lung anti-elastase protection. In the over 800 weekly infusions administered, no significant adverse reactions have occurred. These findings demonstrate that long-term augmentation therapy with weekly infusions of A1AT is a rational, safe, and biochemically effective therapy for A1AT deficiency.

L18 ANSWER 26 OF 29 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 1984278561 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 6380357
TITLE: Emphysema induced by intravenously administered endotoxin in an alpha 1-antitrypsin-deficient rat model.
AUTHOR: Blackwood R A; Moret J; Mandl I; Turino G M
SOURCE: The American review of respiratory disease, (1984 Aug) Vol. 130, No. 2, pp. 231-6.
Journal code: 0370523. ISSN: 0003-0805.

PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198409
ENTRY DATE: Entered STN: 20 Mar 1990
Last Updated on STN: 20 Mar 1990
Entered Medline: 5 Sep 1984

AB The effect of repeated intravenous injections of Escherichia coli endotoxin on lung structure and lung parenchymal elastin proportions was studied in rats rendered deficient in alpha 1-antitrypsin by administration of galactosamine. Within 24 h after endotoxin administration, polymorphonuclear leukocyte sequestration was demonstrable by microscopy and differential cell counts of pulmonary lavage fluid. Measurement of the proportions of elastin in lung parenchyma at 24 h revealed values in the normal range; 10 wk after repeated galactosamine and endotoxin administration, there was a reduction in the proportions of lung parenchymal elastin. At 10 wk, these animals showed a significant increase in the mean linear intercept and pulmonary compliance. Animals treated with endotoxin alone developed some but not all of the changes seen in the animals deficient in alpha 1-antitrypsin.

L18 ANSWER 27 OF 29 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 1977146111 EMBASE Full-text
TITLE: Effect of new therapeutic agents for pancreatitis on serum alpha(1) antitrypsin and alpha(2) macroglobulin in humans (Japanese).
AUTHOR: Nakajima, S.; Ito, M.; Mizuno, F.; Nakano, H.
CORPORATE SOURCE: Dept. Int. Med., Fujita Gakuen Univ., Sch. Med., Toyoake, Japan.
SOURCE: Japanese Journal of Gastroenterology, (1976) Vol. 73, No. 6, pp. 668-676.
ISSN: 0446-6586 CODEN: NIPAA4
DOCUMENT TYPE: Journal
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: Japanese

AB A synthetic protease inhibitor, ethyl P (6 guanidino hexanoyloxy) benzoate methanesulfonate (FOY), and chlorophyll a have been proposed recently as potential therapeutic agents for acute pancreatitis. To define the mechanisms involved, serum alpha(1) antitrypsin, alphamacroglobulin and amylase were determined before and after the administration of these agents in humans. Serum alpha(1) antitrypsin and alpha(2) macroglobulin levels assayed by single radial immunodiffusion were significantly increased by intravenous injections of 100 mg FOY in normal control subjects. Daily intravenous infusions of 200 mg FOY for 12 days were effective in the treatment of acute pancreatitis, causing 29% increase in serum alpha(1) antitrypsin and a marked reduction in urinary isoamylase of pancreatic type as well as in serum γ glutamyl transpeptidase. In patients with chronic pancreatitis, oral administrations of 1800 mg FOY per day for 2 weeks had little effects on serum alpha(1) antitrypsin, alpha(2) macroglobulin and hourly rate of urinary amylase excretion. No significant correlation was demonstrated between serum alpha(1) antitrypsin and alpha(2) macroglobulin levels. Intravenous injections of 20 mg chlorophyll a had no effects on serum alpha(1) antitrypsin and alpha(2) macroglobulin levels in control subjects. These results indicate that the mechanisms of action of the 2 agents are different.

L18 ANSWER 28 OF 29 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 1975026320 EMBASE Full-text
TITLE: [The serum levels alpha(1) antitrypsin and alpha(2) macroglobulin in the human being after intravenous injection of 25,000 I.U. Trasylol].
DAS VERHALTEN VON ALPHA(1) ANTITRYPSIN UND ALPHA(2) MACROGLOBULIN BEIM MENSCHEN NACH I.V. INJEKTION VON 25 000 IE TRASYLOL.
AUTHOR: Cegla, U.H.; Huebner, M.
CORPORATE SOURCE: Abt. Pneumol., Johann Wolfgang Goethe Univ., Frankfurt/M., Germany.
SOURCE: Klinische Wochenschrift, (1974) Vol. 52, No. 11, pp. 553-554.
ISSN: 0023-2173 CODEN: KLWOAZ
DOCUMENT TYPE: Journal
FILE SEGMENT: 025 Hematology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
006 Internal Medicine
LANGUAGE: German
AB The levels of alpha(1) antitrypsin and alpha(2) macroglobulin in 5 male patients (age 30 to 45 yr) with exudative tuberculosis of the lung were examined before and after i.v. injection of 25000 I.U. of Trasylol by the radio immunodiffusion method of Mancini. Three, 6 and 9 hr after the injection the serum levels of the alpha antitrypsin and alpha(2) macroglobulin were significantly (P<0.01 combined alpha(1) t Test) greater than the controls.

L18 ANSWER 29 OF 29 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1960:10046 BIOSIS Full-text
DOCUMENT NUMBER: PREV19603500010049; BA35:10049
TITLE: Changes of the serum antitrypsin in rabbits with experimental nephritis and in rabbits in the same condition which were treated with trypsin [With Czech, Russian and English summ.].
Original Title: Variations de l'anti-trypsine serique apres l'application intraveineuse de la trypsine chez les lapins ayant la nephrite expe'rimentale [With Czech, Russian and English summ.].
AUTHOR(S): POLAK, J.; VOTAVA, L.; EVELOVA, D.; EVELA, M.; SKALOVA, M.
CORPORATE SOURCE: U. Masaryk, Brno, Czechoslovakia
SOURCE: SCRIPTA MED [BRNO], (1959) Vol. 32, No. 1, pp. 1-6.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: Unavailable
ENTRY DATE: Entered STN: May 2007
Last Updated on STN: May 2007
AB Changes of serum antitrypsin were observed in rabbits subjected to experimental nephritis and in those which in the same condition were treated with trypsin. In both groups a rise could be observed, the climax in the first being on the 4th day, while in the 2d on the 7th day of illness. The subsequent rise of serum antitrypsin in the course of experimental nephritis,

influenced by trypsin administered intravenously is ascribed to the effect of trypsin on the course of the inflammation. ABSTRACT AUTHORS: Auth. summ

(FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, WPIX, JAPIO, PASCAL, DISSABS, LIFESCI, BIOTECHDS, SCISEARCH, BIOTECHNO, PROMT, RDISCLOSURE' ENTERED AT 15:59:58 ON 18 MAY 2009)

L19 8236 S "SHAPIRO L"?/AU
L20 3 S L19 AND L4
L21 3 DUP REM L20 (0 DUPLICATES REMOVED)

L21 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:1279575 HCAPLUS Full-text
DOCUMENT NUMBER: 149:486823
TITLE: Compositions and methods of use for alpha-1 antitrypsin having no significant serine protease inhibitor activity
INVENTOR(S): Shapiro, Leland
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 24pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20080261869	A1	20081023	US 2008-106052	20080418
WO 2009005877	A2	20090108	WO 2008-US60848	20080418
WO 2009005877	A3	20090305		

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2007-913174P P 20070420

AB Embodiments herein illustrate methods and compns. for treating medical disorders. In certain embodiments, compns. and methods relate to reducing, inhibiting or treating a bacterial infection, or a viral infection in a subject. More particularly, embodiments herein relate to compds. including naturally occurring and synthetic compns. having α-1 antitrypsin activity but no significant serine protease inhibitor activity.

L21 ANSWER 2 OF 3 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:362731 BIOSIS Full-text
DOCUMENT NUMBER: PREV200600351937
TITLE: A novel antiapoptotic role for alpha(1)-antitrypsin in the prevention of pulmonary emphysema.

AUTHOR(S): Petrache, Lrina [Reprint Author]; Fijalkowska, Lwona; Zhen, Lijie; Medler, Terry R.; Brown, Emile; Cruz, Pedro; Choe, Kang-Hyeon; Taraseviciene-Stewart, Laimute; Scerbavicius, Robertas; Shapiro, Lee ; Zhang, Bing; Song, Sihong; Hicklin, Dan; Voelkel, Norbert F.; Flotte, Terence; Tuder, Rubin M.

CORPORATE SOURCE: Indiana Univ, 1481 W 10th St,111P-IU, Indianapolis, IN 46202 USA
ipetrach@iupui.edu

SOURCE: American Journal of Respiratory and Critical Care Medicine, (JUN 1 2006) Vol. 173, No. 11, pp. 1222-1228. ISSN: 1073-449X.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 19 Jul 2006
Last Updated on STN: 19 Jul 2006

AB Rationale: There is growing evidence that alveolar cell apoptosis plays an important role in emphysema pathogenesis, a chronic inflammatory lung disease characterized by alveolar destruction. The association of alpha(1)-antitrypsin deficiency with the development of emphysema has supported the concept that protease/antiprotease imbalance mediates cigarette smoke-induced emphysema.Objectives: We propose that, in addition to its antielastolytic effects, alpha(1)-antitrypsin may have broader biological effects in the lung, preventing emphysema through inhibition of alveolar cells apoptosis.Methods, Measurements, and Main Results: Transduction of human alpha(1)-antitrypsin via replication-deficient adeno-associated virus attenuated airspace enlargement and emphysema caused by inhibition of vascular endothelial growth factor (VEGF) receptors with SU5416 in mice, a model of apoptosis-dependent emphysema lacking neutrophilic inflammation. The overexpressed human serine protease inhibitor accumulated in lung cells and suppressed caspase-3 activation and oxidative stress in lungs treated with the VEGF blocker or with VEGF receptor-1 and -2 antibodies. Similar results were obtained in SU5416-treated rats given human alpha(1)-antitrypsin intravenously.Conclusions: Our findings suggest that inhibition of structural alveolar cell apoptosis by alpha(1)-antitrypsin represents a novel protective mechanism of the serpin against emphysema. Further elucidation of this mechanism may extend the therapeutic options for emphysema caused by reduced level or loss of function of alpha(1)-antitrypsin.

L21 ANSWER 3 OF 3 WPIX COPYRIGHT 2009 THOMSON REUTERS on STN

ACCESSION NUMBER: 2005-272817 [28] WPIX

DOC. NO. CPI: C2005-085234 [28]

TITLE: Method for treating bacterial infection in mammal, involves administering composition comprising substance exhibiting mammalian alpha-antitrypsin or serine protease inhibitor, and excipient

DERWENT CLASS: B04; D16

INVENTOR: SHAPIRO L

PATENT ASSIGNEE: (SHAP-I) SHAPIRO L; (COLS-C) UNIV COLORADO

COUNTRY COUNT: 107

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005019434	A2	20050303	(200528)*	EN	78[5]	
US 20050106151	A1	20050519	(200534)	EN		
EP 1660094	A2	20060531	(200636)	EN		
JP 2007504144	W	20070301	(200718)	JA	52	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005019434 A2		WO 2004-US27711	20040826
US 20050106151 A1	Provisional	US 2003-497703P	20030826
EP 1660094 A2		EP 2004-801916	20040826
US 20050106151 A1		US 2004-926051	20040826
EP 1660094 A2		WO 2004-US27711	20040826
JP 2007504144 W		WO 2004-US27711	20040826
JP 2007504144 W		JP 2006-524842	20040826

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1660094	A2	Based on	WO 2005019434	A
JP 2007504144	W	Based on	WO 2005019434	A

PRIORITY APPLN. INFO: US 2003-497703P 20030826
US 2004-926051 20040826

AN 2005-272817 [28] WPIX

AB WO 2005019434 A2 UPAB: 20051222

NOVELTY - Treatment of bacterial infection in a mammal involves administering a pharmaceutical composition comprising substance exhibiting mammalian alphal-antitrypsin or inhibitor of serine protease activity or a functional derivative, and excipient.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) relieving or ameliorating pain or symptoms associated with bacterial diseases or indications in mammal suffering from mycobacterial diseases or indications, which involves administering the pharmaceutical composition;

(2) treatment of mycobacterial infection in mammal and method of relieving or ameliorating pain or symptoms associated with mycobacterial diseases, which involves administering the composition; (3) inhibition of mycobacterial infection of macrophages in mammal, which involves administering mammalian alpha-antitrypsin or serine protease inhibitor to the mammal susceptible to mycobacterial colonization of macrophages;

(4) preventing deficiency of functional endogenous alpha-antitrypsin levels in mammal susceptible to mycobacterial infection mediated by endogenous host serine protease or serine protease like activity, which involves treating the mammal with the pharmaceutical composition; and

(5) prevention of anthrax symptoms due to Bacillus anthracis, which involves administering substance exhibiting mammalian alphal-antitrypsin or serine protease inhibitor for blocking endogenous host protease cell surface processing of inactive large PA into active smaller PA molecule.

ACTIVITY - Antimicrobial; Antibacterial; Antiulcer; Antiinflammatory; Respiratory-Gen.; Antitussive; Immunosuppressive. No biological data given.

MECHANISM OF ACTION - Cytokine-Antagonist; IL-Antagonist-1; TNF-Antagonist-Alpha; IL-Antagonist-18; Nitric-oxide-Antagonist (all claimed).

Effect of alpha 1-antitrypsin on Mycobacterium avium complex infection was evaluated using human monocyte-derived macrophages (MDM) isolated from human peripheral blood mononuclear cells. MDM were infected with Mycobacterium avium (9141) strain and incubated for 1 hour. The supernatant was then removed and cytokine assays were performed. Alpha 1-antitrypsin significantly blocked infection of MDM with the strain, with a mean effect of 55%. The result concluded that alpha 1-antitrypsin exhibited excellent serine protease inhibition effect.

USE - For preventing and treating bacterial infection (mycobacterial infection), anthrax, cutaneous ulceration, edema, scar formation and

inhalation anthrax, and anthrax symptoms such as pulmonary edema, lymphaonaphy, pleural effusion, ventirolatory compromise, cough, sweating, rigors and septic shock (claimed).
ADVANTAGE - The method enables effective inhibition of serine protease, and reduction or inhibition of pain and/or symptoms associated with bacterial indication(s) is in the order of 10-20%, 30-40%, 50-60% or 75-100% reduction and inhibition (claimed). The composition is highly effective against gram negative, gram positive and acid-fast bacilli, and enables modulation of cellular activities including macrophage activity and inhibition of toxin.
DESCRIPTION OF DRAWINGS - The graph shows the effect of alpha 1-antitrypsin on Mycobacterium avium complex infection of human monocyte-derived macrophages.

FILE 'HOME' ENTERED AT 16:04:23 ON 18 MAY 2009

```
=> d his ful

     FILE 'REGISTRY' ENTERED AT 14:15:09 ON 18 MAY 2009
L1           20 SEA ABB=ON  PLU=ON  "A1-ANTITRYPSIN"?/CN

     FILE 'HCAPLUS' ENTERED AT 14:15:43 ON 18 MAY 2009
L2        10337 SEA ABB=ON  PLU=ON  L1 OR (A1 OR ALPHA1 OR (ALPHA OR
                A)(1A)1)(A)(ANTITRYPSIN OR ANTI(W)(TRYPSIN OR PROTEINASE
                OR PROTEASE) OR ANTIPROTEASE OR ANTIPROTEINASE OR (PROTEASE
                 OR PROTEINASE)(W)INHIBIT?) OR A1PI OR PROLASTIN OR
                ZEMAIRA OR AAT(10A)?TRYPSIN? OR A1AT OR ANTITRYPSIN OR
                ANTI TRYPSIN
L3          392 SEA ABB=ON  PLU=ON  L2(30A)(ADMIN? OR INJECT? OR APPLY? OR
                APPLIED OR APPLICATION)
L4           73 SEA ABB=ON  PLU=ON  L3(30A)(PARENTAL? OR ORAL? OR MOUTH OR
                VAGINAL? OR RECTAL? OR ANAL OR NASAL? OR MOSE OR BUCCAL?
                OR INTRAVENOUS? OR IV OR I V OR INTRA(W)(VENOUS? OR
                MUSCUL? OR CEREBROVENTRIC?) OR INTRAMUSCUL? OR SUBCUTANEOUS
                ? OR INTRATHECAL? OR EPIDURAL? OR TRANSDERMAL? OR INTRACERE
                BROVENTRIC?)
L5            2 SEA ABB=ON  PLU=ON  L3(30A)(OSMOTIC?(W)PUMP OR INHALE# OR
                INHALANT OR INHALING OR INHALATION?)
L6           46 SEA ABB=ON  PLU=ON  (L4 OR L5) AND (PY<2000 OR AY<2000 OR
                PRY<2000)
L7           37 SEA ABB=ON  PLU=ON  L6 AND (PARENTAL? OR ORAL? OR MOUTH OR
                INTRAVENOUS? OR IV OR I V OR INTRA(W)(VENOUS? OR MUSCUL?)
                OR INTRAMUSCUL? OR EPIDURAL?)
L8            9 SEA ABB=ON  PLU=ON  L6 NOT L7

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIX, JAPIO, PASCAL, DISSABS, LIFESCI,
     BIOTECHDS, SCISEARCH, BIOTECHNO, PROMT, RDISCLOSURE' ENTERED AT
     14:24:37 ON 18 MAY 2009
L9           29 SEA ABB=ON  PLU=ON  L8
L10          21 DUP REM L9 (8 DUPLICATES REMOVED)

     FILE 'HCAPLUS' ENTERED AT 14:50:35 ON 18 MAY 2009
                D QUE L4
                D QUE L5
                D L8 1-9

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIX, JAPIO, PASCAL, DISSABS, LIFESCI,
     BIOTECHDS, SCISEARCH, BIOTECHNO, PROMT, RDISCLOSURE' ENTERED AT
     14:50:36 ON 18 MAY 2009
                D L10 1-21 IBIB ABS

     FILE 'HCAPLUS' ENTERED AT 14:52:47 ON 18 MAY 2009
L11          37 SEA ABB=ON  PLU=ON  L6 NOT L8

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIX, JAPIO, PASCAL, DISSABS, LIFESCI,
     BIOTECHDS, SCISEARCH, BIOTECHNO, PROMT, RDISCLOSURE' ENTERED AT
L12          29 SEA ABB=ON  PLU=ON  L2(10A)((ADMIN? OR INJECT? OR APPLICATI
                ON OR APPLY? OR APPLIED)(10A)(OSMOTIC?(W) PUMP OR INHALE#
                OR INHALANT OR INHALING OR INHALATION?))
L13          42 SEA ABB=ON  PLU=ON  L2(10A)((ADMIN? OR INJECT? OR APPLICATI
                ON OR APPLY? OR APPLIED)(10A)(INTRAMUSCUL? OR SUBCUTANEOUS?
                 OR INTRATHECAL? OR EPIDURAL? OR TRANSDERMAL? OR INTRACEREB
                ROVENTRIC?))
L14         189 SEA ABB=ON  PLU=ON  L2(10A)((ADMIN? OR INJECT? OR APPLICATI
                ON OR APPLY? OR APPLIED)(10A)(PARENTAL? OR ORAL? OR MOUTH
                OR VAGINAL? OR RECTAL? OR ANAL OR NASAL? OR MOSE OR
```

```
                BUCCAL? OR INTRAVENOUS? OR IV OR I V OR INTRA(W)(VENOUS?
                OR MUSCUL? OR CEREBROVENTRIC?)))
L15         243 SEA ABB=ON  PLU=ON  ((L12 OR L13 OR L14)) NOT L9
L16         117 SEA ABB=ON  PLU=ON  L15 AND (PY<2000 OR AY<2000 OR
                PRY<2000)
L17          63 SEA ABB=ON  PLU=ON  L16 AND (TREAT? OR THERAP? OR PREVENT?)
L18          29 DUP REM L17 (34 DUPLICATES REMOVED)

     FILE 'HCAPLUS' ENTERED AT 15:57:36 ON 18 MAY 2009
                D QUE L6
                D L11 1-37

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIX, JAPIO, PASCAL, DISSABS, LIFESCI,
     BIOTECHDS, SCISEARCH, BIOTECHNO, PROMT, RDISCLOSURE' ENTERED AT
     15:57:41 ON 18 MAY 2009
                D L18 1-29 IBIB ABS

     FILE 'HCAPLUS' ENTERED AT 15:58:25 ON 18 MAY 2009
                D QUE L6
                D L11 1-37

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIX, JAPIO, PASCAL, DISSABS, LIFESCI,
     BIOTECHDS, SCISEARCH, BIOTECHNO, PROMT, RDISCLOSURE' ENTERED AT
     15:58:55 ON 18 MAY 2009
                D L18 1-29 IBIB ABS

     FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, WPIX, JAPIO, PASCAL, DISSABS,
     LIFESCI, BIOTECHDS, SCISEARCH, BIOTECHNO, PROMT, RDISCLOSURE' ENTERED
     AT 15:59:58 ON 18 MAY 2009
L19        8236 SEA ABB=ON  PLU=ON  "SHAPIRO L"?/AU
L20           3 SEA ABB=ON  PLU=ON  L19 AND L4
L21           3 DUP REM L20 (0 DUPLICATES REMOVED)
                D 1-3 IBIB ABS

     FILE 'HOME' ENTERED AT 16:04:23 ON 18 MAY 2009


     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:   17 MAY 2009  HIGHEST RN 1147079-26-2
     DICTIONARY FILE UPDATES:  17 MAY 2009  HIGHEST RN 1147079-26-2

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

     TSCA INFORMATION NOW CURRENT THROUGH January 9, 2009.

       Please note that search-term pricing does apply when
       conducting SmartSELECT searches.

     REGISTRY includes numerically searchable data for experimental and
     predicted properties as well as tags indicating availability of
     experimental property data in the original document.  For information
     on property searching in REGISTRY, refer to:

     http://www.cas.org/support/stngen/stndoc/properties.html

     FILE HCAPLUS
```

FILE COVERS 1907 - 18 May 2009 VOL 150 ISS 21
FILE LAST UPDATED: 17 May 2009 (20090517/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2009

HCAplus now includes complete International Patent Classification (IPC reclassification data for the third quarter of 2008.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE MEDLINE
FILE LAST UPDATED: 16 May 2009 (20090516/UP). FILE COVERS 1949 TO DA

MEDLINE and LMEDLINE have been updated with the 2009 Medical Subject Headings (MeSH) vocabulary and tree numbers from the U.S. National L of Medicine (NLM). Additional information is available at

http://www.nlm.nih.gov/pubs/techbull/nd08/nd08_medline_data_changes_2

On February 21, 2009, MEDLINE was reloaded. See HELP RLOAD for detai

This file contains CAS Registry Numbers for easy and accurate substance identification.

See HELP RANGE before carrying out any RANGE search.

FILE BIOSIS
FILE COVERS 1926 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1926 TO DATE.

RECORDS LAST ADDED: 13 May 2009 (20090513/ED)

BIOSIS has been augmented with 1.8 million archival records from 1926 through 1968. These records have been re-indexed to match current BIOSIS indexing.

FILE EMBASE
FILE COVERS 1974 TO 18 May 2009 (20090518/ED)

EMBASE was reloaded on March 30, 2008.

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

Beginning January 2008, Elsevier will no longer provide EMTREE codes as part of the EMTREE thesaurus in EMBASE. Please update your current-awareness alerts (SDIs) if they contain EMTREE codes.

For further assistance, please contact your local helpdesk.

FILE WPIX
FILE LAST UPDATED: 14 MAY 2009 <20090514/UP>
MOST RECENT UPDATE: 200930 <200930/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE
>>> Now containing more than 1.3 million chemical structures in DCR <<

>>> IPC, ECLA and US National Classifications have been updated with reclassifications to March 15th, 2009.
F-Term and FI-Term original classifications are current and reclassification will commence in June.
No update date (UP) has been created for the reclassified documents, but they can be identified by specific update codes (see HELP CLA for details)<<<

FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
http://www.stn-international.com/stn_guide.html

FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomsonreuters.com/support/patents/coverage/latestup

EXPLORE DERWENT WORLD PATENTS INDEX IN STN ANAVIST, VERSION 2.0:
http://www.stn-international.com/DWPIAnaVist2_0608.html

>>> HELP for European Patent Classifications see HELP ECLA, HELP ICO <

FILE JAPIO
FILE LAST UPDATED: 6 MAY 2009 <20090506/UP>
MOST RECENT PUBLICATION DATE: 29 JAN 2009 <20090129/PD>

>>> GRAPHIC IMAGES AVAILABLE <<<

FILE PASCAL
FILE LAST UPDATED: 18 MAY 2009 <20090518/UP>
FILE COVERS 1977 TO DATE.

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION IS AVAILABLE IN THE BASIC INDEX (/BI) FIELD <<<

FILE DISSABS
FILE COVERS 1861 TO 29 APR 2009 (20090429/ED)

```
MATERIALS OR THEIR USE.

FILE LIFESCI
FILE COVERS 1978 TO 1 May 2009 (20090501/ED)

FILE BIOTECHDS
FILE LAST UPDATED: 18 MAY 2009       <20090518/UP>
FILE COVERS 1982 TO DATE

>>> USE OF THIS FILE IS LIMITED TO BIOTECH SUBSCRIBERS <<<


FILE SCISEARCH

FILE COVERS 1974 TO 14 May 2009 (20090514/ED)

SCISEARCH has been reloaded, see HELP RLOAD for details.

FILE BIOTECHNO
FILE LAST UPDATED: 7 JAN 2004       <20040107/UP>
FILE COVERS 1980 TO 2003.
THIS FILE IS A STATIC FILE WITH NO UPDATES

>>>  SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN
     /CT AND BASIC INDEX  <<<

FILE PROMT
 FILE COVERS 1978 TO 16 May 2009 (20090516/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

FILE RDISCLOSURE
FILE LAST UPDATED: 18 MAY 2009       <20090518/UP>
FILE COVERS 1960 TO DATE

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION IS AVAILABLE IN THE
    BASIC INDEX (/BI) AND TITLE (/TI) FIELDS <<<

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

FILE HOME
```